IN THE UNITED STATES DISTRICT COURT

IN AND FOR THE DISTRICT OF DELAWARE

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IN RE BRIMONIDINE PATENT LITIGATION) C.A. 07-md-1866-GMS

- - -

Wilmington, Delaware
Thursday, March 12, 2009
9:00 a.m.
Day 4 of Trial

- - -

BEFORE: HONORABLE GREGORY M. SLEET, Chief Judge

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THE COURT: Good morning.

(Counsel respond "Good morning.)

THE COURT: Mr. Singer, you were up yesterday?

MR. SINGER: Yes, with Mr. Dziabo.

THE COURT: Why don't we resume. Let's go.

MR. BREISBLATT: Your Honor, I think we are beginning cross-examination this morning.

THE COURT: Had you completed, Mr. Singer?

MR. SINGER: Yes, Your Honor.

THE COURT: Re-swear Mr. Dziabo.

ANTHONY J. DZIABO, JR., having been duly sworn as a witness, was examined and testified as followings...

THE COURT: Good morning, Mr. Dziabo.

THE WITNESS: Good morning, Your Honor.

CROSS-EXAMINATION

BY MR. SODIKOFF:

Q. **Mr. Dziabo, do you recall that Frank Uxa was your lawyer in the Patent Office during part of your attempts to get the '078 patent?**

A. **Yes, I do.**

Q. **In fact, he was your lawyer on the appeal you referred to yesterday, wasn't he?**

A. **Yes, I believe that's correct.**

Q. **And that appeal was in the Patent Office, that wasn't**

in the Federal Circuit. Correct?

A. **I believe it was at the Patent Office.**

Q. **Mr. Uxa was paid by Allergan to represent you, wasn't he?**

A. **I believe so.**

Q. **Mr. Dziabo, are you aware of the fact that Mr. Uxa, your legal representative before the United States Patent and Trademark Office, made this statement: "The fact that stabilized chlorine dioxide is a well-known preservative for other applications may make it useful to try to adapt this preservative material to ocular applications"?**

A. **I don't recall where he made that statement.**

MR. SODIKOFF: Your Honor, may I approach the witness and the Bench?

THE COURT: Yes.

MR. SODIKOFF: Your Honor, I have handed up what we have marked as JTX-006A. This is part of the prosecution history of the '078 patent.

BY MR. SODIKOFF:

Q. **This is a filing in your patent application, sir, isn't it? The title at the top there, "Aqueous Ophthalmic Solutions and Methods for Preserving Same"?**

A. **Yes.**

Q. **Let's go to Page 11 of this filing made on behalf of you by your representative at the U.S. PTO. Allergan**

0978373.

Doesn't your lawyer here admit to the U.S. Patent Office, as part of your efforts to procure this patent, that the fact that stabilized chlorine dioxide is a well-known preservative for other applications may make it useful to try to adapt this preservative material to ocular applications?

A. **That's what it reads.**

Q. **So Mr. Uxa, on your behalf, admitted that stabilized chlorine dioxide is a well-known preservative, didn't he?**

A. **Well, I think it's rather --**

Q. **I am sorry, that is a yes or no question, sir.**

A. **Would you repeat the question?**

Q. **Mr. Uxa admitted that stabilized chlorine dioxide is a well-known preservative, didn't he?**

A. **That's what he states here, yes.**

Q. **And are you aware that statements made to the PTO are binding?**

MR. SINGER: Objection, Your Honor. Foundation.

THE COURT: If he is aware.

If you are aware, you are. If you are not --

THE WITNESS: I am --

THE COURT: You don't have guess.

BY MR. SODIKOFF:

Q. **It's a yes or no question, sir.**

A. **No.**

Q. **In fact, are you aware that Mr. Uxa made the same statement not once but twice during the prosecution history, including in the appellate brief?**

A. **No.**

MR. SODIKOFF: Your Honor, may I approach the witness and the Bench?

THE COURT: You may do so freely, counsel.

MR. SODIKOFF: If I can direct the Court to Allergan 098378.

THE COURT: JTX-078 006B?

MR. SODIKOFF: JTX-078 006B, another excerpt from the file history of the '078 patent.

BY MR. SODIKOFF:

Q. **At the top of this document, Mr. Dziabo, you would agree that, on the top left here, it says, "In Re Application of Dziabo, et al"?**

A. **Yes.**

Q. **This is your patent application, sir, isn't it?**

A. **Yes.**

Q. **This document was sent to the notice of appeal, to the Honorable Commissioner of Patents and Trademarks in Washington, wasn't it, sir?**

A. **I would assume so.**

Q. **On the front page, we have a signature by Mr. Uxa, who**

was your attorney. Correct?

A. **Yes.**

Q. **If we can move to Allergan 978398.**

Here again, your attorney states, on your behalf, "The fact that stabilized chlorine dioxide is a well-known preservative for other applications may make it useful to try to adapt this preserve material to ocular applications." Is that correct?

A. **That's correct.**

Q. **Sir, are we now in agreement that your patent attorney repeatedly admitted that stabilized chlorine dioxide was a well-known preservative before you filed your patent application?**

A. **He certainly stated that.**

Q. **Thank you.**

Let's look now at JTX-252. Sir, can you tell me what this is?

A. **This is a United States Patent for No. 4,499,077, Stockel, et al.**

Q. **And the Stockel, et al. Patent, if we can call it up, DTX-252, the date of that patent is February 12, 1985. Is that correct?**

A. **That's correct.**

Q. **And you do not dispute that this patent is prior art to your patent, do you? Looks like? Do you dispute that,**

sir?

A. Yes, I do.

Q. You dispute that this patent is prior art?

A. Yes, I do.

Q. Do you know what the term "prior art" means, sir?

A. I believe I do.

Q. Was this patent issued on February 12th, 1985?

A. It so reads.

Q. Do you have any reason to dispute that this government-issued paper was not, in fact, issued on February 12th, 1985?

A. No.

THE COURT: He says he disagrees with you on that, he disagrees with the characterization of the document as prior art.

BY MR. SODIKOFF:

Q. Can you explain to me why you think this is not prior art?

A. Well, if this is the patent I am thinking of, this particular patent describes the use of an antimicrobial composition for the use of contact lenses.

Q. I am sorry. I think you might be confused on what prior art is.

THE COURT: I don't think he is confused. I think you should let him finish his interest.

Go ahead and finish your answer.

THE WITNESS: If you give me a moment to read the abstract.

THE COURT: Go right ahead, Mr. Dziabo.

THE WITNESS: Okay, your question again?

BY MR. SODIKOFF:

Q. **I withdraw my question.**

Mr. Dziabo, would you agree that this document was published more than one year before you filed your patent application?

A. **Yes.**

Q. **Let's look at Column 12, beginning at Line 20 through 28. Do you see here where it talks about the antimicrobial effectiveness of the combination of IL-779 and stabilized chlorine dioxide?**

A. **Yes, I do.**

Q. **Do you see where it states that the lowest concentration of this combination resulting in complete inhibition of visible growth for 48 hours represents the minimum inhibition concentration, abbreviated "MIC," value?**

Do you see that?

A. **Yes.**

Q. **And the next sentence says that these values are intended to be used as an index of efficacy for preservative applications, doesn't it?**

A. **Yes.**

Q. **And according to your lawyer, and his admissions in the '078 patent prosecution history, we know that stabilized chlorine dioxide was a known preservative. Correct?**

A. **That's what was stated in the patent.**

Q. **Now, if we move on, move to Column 11 of this patent, the 077 Stockel, in the table on the left, the paragraph just before it -- the last table, Line 45 through 55. We find here a solution described, don't we, sir?**

A. **Yes.**

Q. **And this solution includes stabilized chlorine dioxide, does it not?**

A. **Yes, it does.**

Q. **And this solution contains sodium chloride, sir. Is that correct?**

A. **Yes, it does.**

Q. **And the solution contains boric acid. Is that correct?**

A. **Yes, it does.**

Q. **And this solution is at a pH of 7.0. Is that correct?**

A. **Yes, it is.**

Q. **The concentration of stabilized chlorine dioxide, .005 percent, is the same concentration that you describe in your patent, isn't it?**

A. **Yes.**

THE COURT: Do you need a moment, counsel?

MR. SODIKOFF: Just one second, please.

THE COURT: All right.

MR. SODIKOFF: Thank you, I am sorry.

BY MR. SODIKOFF:

Q. **Now, this solution that we see here in the Stockel '077 patent, it states that it's for use in sterilizing contact lenses. Is that correct? Line 46, Column 11.**

A. **Yes, it does say that.**

Q. **And this solution that is used to sterilize contact lenses contains the same concentration of stabilized chlorine dioxide as the concentration that you describe in your patent. Isn't that correct?**

A. **That's correct.**

MR. SODIKOFF: Your Honor, can I have one second?

THE COURT: Sure.

(Pause.)

BY MR. SODIKOFF:

Q. **If we can go to the '078 patent, JTX-001.**

MR. SODIKOFF: May I approach, Your Honor.

THE COURT: Yes, you may.

BY MR. SODIKOFF:

Q. **This is your patent, isn't it, sir?**

A. **Yes, it is.**

Q. **I would like to look at Example 1, Column 7 of this patent, and I would like to look specifically at Lines 25 through 42 -- actually, through 48.**

Does this table describe a solution that you have referred to as a borate buffered saline solution?

A. **Yes, it does.**

Q. **And this is a stock solution within Allergan, is it not?**

A. **I wouldn't characterize it as a stock solution. But it is a typical solution that is used as a vehicle for ophthalmic products?**

Q. **It is a typical vehicle used in ophthalmic products both inside and outside of Allergan. Correct?**

A. **I can't speak for outside of Allergan.**

Q. **Well, there is nothing unusual about that solution, is there, sir?**

A. **Unusual in what way?**

Q. **It's not unique in any way, is it?**

A. **It's typical.**

Q. **And, indeed, it is a solution that Allergan had been using for some time as a base for products, for ophthalmology products. Correct?**

A. **For ophthalmic products, yes.**

Q. **And the borate buffered solution is a standard vehicle that Allergan used. Is that correct?**

A. **It is a vehicle that was used, yes.**

Q. **And it's in the physiological range for tonicity, sir?**

A. **This solution would yield an isotonic solution.**

Q. **And an isotonic solution is the same as the tonicity in the eye. Is that correct?**

A. **That's correct.**

Q. **Below, it says that, in this patent, you used the hydrochloric acid or sodium hydroxide to adjust the pH?**

That wasn't something that was unique to Allergan, was it, sir?

A. **No, it was not.**

Q. **Adjusting the pH through this manner was well-known in the art, wasn't it?**

A. **That is typical pharmaceutical technique.**

Q. **Known both to those inside and outside of Allergan. Correct?**

A. **Correct.**

Q. **And actually creating this basic borate buffered saline solution is also within the skill of the art of those both inside and outside of Allergan. Isn't that correct, sir?**

A. **Yes.**

Q. **And the pH chosen here of about 7.7 to 7.9, that's within .3 or .4 of what you referred to as physiological pH of the eye. Isn't that correct, sir?**

A. **Yes.**
Q. **Sir, are you aware that Allergan was selling a thimerisol preserved saline solution out on the market at least one year before the filing of your patent application in 1989?**
A. **Yes.**
Q. **Are you aware that this thimerisol preserved saline solution used thimerisol as a preservative?**
A. **Yes.**
Q. **In fact, this was one of Allergan's biggest sellers, wasn't it?**
A. **I can't recall where it ranked as products for Allergan.**
Q. **Well, it was a preserved saline solution, it was referred to as "the green bottle." Does that ring a bell?**
A. **Yes.**
Q. **And would you disagree with Mr. Ripley if, during his deposition, he stated that this thimerisol preserved saline solution was a big seller for Allergan before 1989?**
A. **You know, I just can't speak to the magnitude or the sales volume. But it was a good product for Allergan.**
Q. **And you wouldn't dispute what Mr. Ripley said, would you?**
A. **No.**
Q. **Are you aware of what the components were in**

Allergan's big selling thimerisol preserved saline solution?

A. **I can't recall exactly today. I was aware at the time, I am sure.**

Q. **This thimerisol preserved saline solution was on sale well before 1989. Isn't that correct?**

A. **I believe so, yes.**

Q. **Would you dispute it if Mr. Ripley said that the preserved thimerisol solution was thimerisol at a low concentration, sodium chloride, and a borate buffer?**

A. **No, I would not dispute that.**

Q. **Would you dispute that Mr. Ripley's best recollection was that the thimerisol preserved saline solution had a target pH of 7.3?**

MR. SINGER: I would okay object to the --

THE COURT: I would sustain the objection to the form of that question.

MR. SINGER: Thank you.

BY MR. SODIKOFF:

Q. **Did the thimerisol preserved saline situation, to your knowledge, have a target pH of 7.3?**

A. **I would say that the -- I would expect that product to have had a pH in the physiological range. I cannot speak to the exact pH value for that product. It's been a while.**

Q. **Would you dispute Mr. Ripley's best recollection that the thimerisol preserved saline solution had a target pH of**

7.3?

A. **No, I would not.**

Q. **So the preserved saline solution, the thimerisol preserved saline solution, was thimerisol, buffer, and the tonicity agent, salt. Is that correct?**

A. **Sodium chloride would be more precise. Yes.**

Q. **And looking back at your patent, in Column 7, Lines 35 to 40, that table, aside from the thimerisol preservative, the other ingredients there are the exact same, aren't they?**

A. **I don't know at this point in time. I haven't seen that formulation in some time. There could be other agents in that solution. Thimerisol was very typically formulated with EDTA, ethylenediaminetetraacetic acid, to help its antimicrobial activity. My recollection is weak on the exact formula. So I can't say that they were identical.**

Q. **Well, let's look at Mr. Ripley's deposition. You can see if you dispute what he said.**

MR. SINGER: I am going to object. That is an improper use.

THE COURT: That is improper. I agree. Sustained.

BY MR. SODIKOFF:

Q. **Let's look at Mr. Ripley's deposition and see if it refreshes your recollection, sir.**

MR. SINGER: Your Honor, this is not

impeachment. He wasn't at Mr. Ripley's deposition. This is not a proper use of deposition testimony.

THE COURT: I agree. Sustained.

I sustained the objection, counsel. Move on.

BY MR. SODIKOFF:

Q. Please look at DTX-357, which I just handed to the witness on the screen.

Mr. Ripley, have you ever seen these proposed rules at the Department of Health & Human Services?

I am sorry, Mr. Dziabo. I apologize.

Have you seen these proposed rules before, sir?

A. I can't recall at the moment.

Q. Would you agree with me that these rules were published in the C.F.R. on Tuesday, June 28th, 1983?

A. It so reads.

Q. And this is, under the action, it is a "Notice of Proposed Rulemaking." Is that correct, sir?

A. That's how it's defined, titled, yes.

Q. If we can go to Page 2 --

A. Page 2 of the document?

Q. Yes. Page 2 of the document, AI 26803. The second paragraph, the second-to-last sentence.

A. Second-to-last sentence.

Q. Where it starts with, "In response."

Would you agree with me that this says that, "In

response to the advance notice of proposed rulemaking, one drug manufacturers' association, five drug manufacturers, and many individual consumers submitted comments"?

A. **Yes.**

Q. **If I can turn to AI 26824. I would like to look at the definitions, specifically, definition F?**

Do you see here where this government-published document defines eyewash, eye lotion, irrigating solution, as a sterile aqueous solution containing no pharmacologically active ingredients, intended for bathing or mechanically flushing the eye?

A. **Yes.**

Q. **Can we turn to AI 00026827.**

I would like to look specifically at 21 C.F.R., Section 349.20, entitled "Eyewashes."

Do you see here, sir, that this is a definition by the FDA in this published document of what an eyewash should be?

A. **Yes.**

Q. **And this was published in 1983. Is that correct?**

A. **Yes.**

Q. **It states that, "These products contain no pharmacologically active ingredients, but contain water, tonicity agents to establish isotonicity with tears, agents for establishing pH and buffering to achieve the same pH as**

tears, and a suitable preservative agent"?

Is that correct?

A. **It so reads.**

Q. **And your thimerisol preserved saline solution would meet this definition, wouldn't it, sir?**

A. **Yes.**

Q. **So now we have both the FDA with this directive and you have an actual product that contains a suitable preservative, tonicity agents to establish isotonicity with tears, and agents for establishing pH and buffering to achieve the same pH. Is that correct, sir?**

A. **Yes.**

Q. **If we could turn back to the '078 patent. Let's look at Claim 1 for a second?**

Let's look at, after the language "therefore comprising."

First, we have described here the stabilized chlorine dioxide. Correct, sir?

A. **Let me catch up with you. Where is that?**

Q. **We are in the '078 patent. JTX-1. For me, that is Column 11, Line 65?**

A. **Column 11, Line 65. I am there. You addressed a particular portion of that.**

Q. **If you look on the screen, I think he is building all of Claim 1, so we can see it together.**

A. **Okay.**

Q. **We are in Claim 1. Right, sir?**

A. **Yes.**

Q. **I am looking, after the term "comprising"?**

A. **Okay. I am with you now.**

Q. **So the first part of this formulation is "stabilized chlorine dioxide in an amount effective to act as a sole preservative."**

Is that correct, sir?

A. **Correct.**

Q. **The second part of your formulation is "one ophthalmically acceptable buffer component in an amount effective to maintain said aqueous ophthalmic formulation at a pH in the range of about 6.8 to 8." Is that correct, sir?**

A. **That's correct.**

Q. **You would agree that 6.8 to 8 is intended to be at the same pH of the human eye; is that correct, sir?**

A. **That's correct.**

Q. **And the use of a buffer component to maintain the pH at this level was specifically provided for in the FDA's definition of an eyewash, wasn't it, sir?**

A. **It was part of the definition for the eyewash, yes.**

Q. **Let's look at the next part: At least one ophthalmically acceptable tonicity component in an amount effective to maintain said aqueous ophthalmic formulation at**

an osmolarity of at least about 200 million licensee Osmol per kilogram?

Did I read that correctly, sir?

A. **Yes.**

Q. **The reason you wanted it at this osmolality is because that's the osmolality, or at least getting closer to the osmolality of the human tear. Is that correct, sir?**

A. **It is the range of the physiology of the eye, yes.**

Q. **Having a tonicity component to get into this range of the human eye was again specifically disclosed in the definition of an eyewash in the FDA regulation. Is that correct?**

A. **Yes.**

Q. **I would like to now talk about the preservative, stabilized chlorine dioxide, because the other two elements were clearly required by the FDA in their definition for eyewash, weren't they, sir?**

A. **In the definition for eyewash, yes.**

Q. **I believe, yesterday, you gave us what you thought was your invention and what your private thoughts were regarding what stabilized chlorine dioxide was. But I would like to look at what you disclosed and gave the public notice of in your patent.**

If we turn to Column 3 -- we are still in JTX-1 -- Column 3, Line 41 through 50, about, just above the

50, where the period is.

This is in your patent. Is that not correct, sir?

A. **Yes, it is.**

Q. **And here, you tell the public that, "The term 'stabilized chlorine dioxide' is well-known in the industry and by those skilled in the art."**

Is that correct?

A. **That's correct.**

Q. **And, earlier, we established that your attorney admitted that stabilized chlorine dioxide was a well-known preservative. Is that correct, sir?**

A. **That's what he stated.**

Q. **And, next, it provides what stabilized chlorine dioxide includes, does it not?**

A. **The next line, yes.**

Q. **And it says, "one or more chlorine dioxide precursors," "one or more." Correct, sir?**

A. **Yes.**

Q. **..."such as one or more chlorine dioxide-containing complexes." Is that correct, sir?**

A. **Correct.**

Q. **..."and/or one or more chlorite containing components."**

Is that correct, sir?

A. **Yes.**

Q. **..."and/or one or more other entities capable of decomposing or being decomposed in a liquid, preferably aqueous, medium to form chlorine dioxide."**

Is that correct, sir?

A. **Yes.**

Q. **And Purogene, the product that was sold by Bio-Cide, fits within this definition, doesn't it, sir?**

A. **Yes, it does.**

Q. **In fact, if we look at Line 59 through 69 of this patent, you tell people, the public, where we can get this stabilized chlorine dioxide, don't you, sir?**

A. **Yes.**

Q. **You tell the public that, "A commercially available stabilized chlorine dioxide which can be utilized in the practice of the present invention is the proprietary stabilized chlorine dioxide of Bio-Cide International, Inc. of Norman, Oklahoma, sold under the trademark Purogene." Is that correct, sir?**

A. **Yes.**

Q. **Then you actually provide for other suitable stabilized chlorine dioxide products, including those -- and I will just summarize here -- called Dura Klor, by Rio Linda Chemical Company. Is that correct, sir?**

A. **Yes.**

Q. **And you also disclose that, for you, stabilized chlorine dioxide also includes what was sold under the trademark Anthium Dioxcide by International Dioxide, Inc. Is that correct?**

A. **Yes.**

Q. **So, in this paragraph, you tell the public that Purogene is a form of stabilized chlorine dioxide. Is that correct?**

A. **That's correct.**

Q. **And you tell the public that Dura Klor is a form of stabilized chlorine dioxide. Is that correct?**

A. **Yes.**

Q. **And you also tell the public that anthium dioxcide is a form of stabilized chlorine dioxide as claimed in your invention. Is that correct?**

A. **Yes.**

Q. **Are you aware that, inside Allergan, Purogene is referred to as Purite?**

A. **Yes.**

Q. **But there is no difference between Purogene and Purite, is there, sir?**

A. **Not to my knowledge.**

Q. **And you didn't play any part in formulating Purogene, itself, did you, sir?**

A. **No.**

Q. **And no one at Allergan played any part in formulating Purogene, to your knowledge, did they, sir?**

A. **To my knowledge, no.**

Q. **And you never directed Bio-Cide to make any changes to Purogene itself to make it more stable, did you, sir?**

A. **Particularly to make the product more stable, we did not direct Bio-Cide to make any changes to the formula.**

MR. SODIKOFF: If I can step away for one second, Your Honor.

Your Honor, may I approach again?

THE COURT: You have free leave, counsel.

MR. SODIKOFF: Thank you.

BY MR. SODIKOFF:

Q. **Mr. Dziabo, I just handed you what has been marked as DTX-216. Is that correct?**

A. **Yes.**

Q. **If we can blow up the body of this letter.**

Can you tell me, sir, do you recognize, sir, looking at the full body of this letter, actually, sir, first, that this letter is from Bio-Cide Chemical Company, Inc.?

A. **Yes.**

Q. **And it was sent to Allergan on March 2nd, 1983?**

A. **That's the date of the letter.**

Q. **When did you start working at Allergan, sir?**

A. **July, I believe it was July 4th -- no. Immediately after the July 4th holiday of 1983.**

Q. **So this letter was sent to Allergan before you arrived at the company. Is that correct?**

A. **That would be correct.**

Q. **I would like to go to the second paragraph. Here it states that, "The purpose of this communication is to introduce our product, Purogene, as a replacement for your disinfectant, Quaternium, and your preservative, thimerisol. Is that correct, sir?**

A. **It so reads.**

Q. **At this time, as we established earlier, Allergan was selling a thimerisol preserved saline solution. Isn't that correct, sir?**

A. **Yes, but that solution did not contain --**

Q. **I am sorry. Yes or no, sir?**

A. **Yes.**

Q. **If we can go back to the '078 patent.**

JTX-001.

I would like to look at Example 5, in Column 8. I would like to compare that to the base solution that we saw in Example 1. So, on the top here, sir, we have the buffered saline solution. Is that correct?

A. **That's correct.**

Q. **And that was a stock saline solution at Allergan. Is**

that correct?
A. That was a typical vehicle used at Allergan. Again, your terminology "stock" --
Q. I apologize. It was a typical vehicle used at Allergen. Is that correct?
A. Yes.
Q. And looking below, ignoring for a second the stabilized chlorine dioxide, you would admit that the other three ingredients are exactly what you would see in the typical buffered saline solution. Is that correct, sir?
A. Yes.
Q. The only addition to get your preservative, preserved saline solution is to put in some stabilized chlorine dioxide. Is that correct?
A. Yes.
Q. Expanding on what we talked about earlier, in order to get this second solution, the preserved saline, you would take some Purogene and put it in this stock saline solution. Isn't that correct, sir?
A. Yes, that's the technique for formulating.
Q. And Purogene, at this time, was literally available at Sears, was it not, sir?
A. That's not a very correct characterization.
Q. Was it or was it not available at Sears, sir?
A. I have no idea. I would not expect it to be so.

MR. SODIKOFF: I will move on, Your Honor.

BY MR. SODIKOFF:

Q. **Now, Example 5 that we just looked at, the same vehicle was also used, or the same buffered saline solution that was typically used at Allergan was also used in Examples 6 and 7. Isn't that correct, sir?**

A. **Yes.**

Q. **And all of these are Purogene .005, sodium chloride as a tonicity agent, boric acid as a buffer, and purified water. Is that correct, sir?**

A. **Yes.**

Q. **I believe that once you make this solution, you tested it for antimicrobial activity. Is that correct?**

A. **That was part of the testing regimen, yes.**

Q. **And you have heard of the U.S. Pharmacopeia. Is that correct, Mr. Dziabo?**

A. **Yes.**

Q. **In common parlance, is it referred to as the USP?**

A. **Correct.**

Q. **Do you mind if I use that abbreviation, sir?**

A. **Please do.**

Q. **The USP requirements for a preservative were known to the public before 1989. Isn't that correct, sir?**

A. **That's correct.**

Q. **And the USP was kind of known as the benchmark adopted**

by the FDA for a preservative. Isn't that correct, sir?

A. **That's correct.**

Q. **And the USP provides specific protocols for testing for preservative effectiveness. Isn't that correct, sir?**

A. **That's correct.**

Q. **Now, Mr. Dziabo, you did not actually conduct in the laboratory the preservative testing. Is that correct?**

A. **Myself personally?**

Q. **Correct.**

A. **That's correct.**

Q. **Lab technicians at Allergan did that. Is that correct?**

A. **The Allergan research microbiology department, who is skilled and trained in these techniques, performed the testing.**

Q. **Well, you haven't listed any of the lab technicians as an inventor here, have you, sir?**

A. **No, we have not.**

Q. **The only inventors listed on the '078 patent are you and Mr. Ripley. Is that correct?**

A. **That's correct.**

Q. **So actually conducting the preservative testing isn't anything that is inventive, is it, sir?**

A. **No. Those are standard protocols.**

Q. **I believe you mentioned yesterday that Allergan also**

conducted toxicology tests of a preservative. Is that correct?

A. **That's correct.**

Q. **Toxicology studies of this specific formulation, sir?**

A. **That's correct.**

Q. **The toxicology studies were not actually performed by you, were they, sir?**

A. **That's correct.**

Q. **They were, again, performed by others within Allergan, presumably, in the toxicology department?**

A. **That's correct.**

Q. **And no one in the toxicology group is listed as an inventor. Is that correct, sir?**

A. **That's correct.**

Q. **So actually conducting toxicology tests is nothing that was new, was it, sir?**

A. **That's correct.**

MR. SODIKOFF: I would like to hand Exhibit 215 -- I am sorry, Exhibit 118 to the defendant, Your Honor?

MR. SINGER: I don't think Mr. Dziabo is on trial for anything, Your Honor.

MR. SODIKOFF: I apologize, Your Honor. I have been watching too many court shows.

BY MR. SODIKOFF:

Q. **This is the Radcliff '215 patent, sir. Can you tell**

me what date this patent was issued?
A. August 25th, 1987.
Q. And this patent was also issued before -- more than one year before you filed your application. Isn't that correct, sir?
A. Yes.
Q. Looking at Column 2 of this patent, if we can look at the bottom half -- actually, just the last sentence, the last two sentences, can you read for me what that says, sir? The second-to-last sentence starting with "a form of."
A. "A form of stabilized chlorine dioxide usable with the present invention is sold under the trademark PUROGENE by Oxyfresh USA, Inc. It is to be noted that the Purogene stabilized chlorine dioxide may be purchased from any service center of the Sears department stores."
Q. If we can move further within Radcliff, sir.
If we can look at Column 11 of the '215 patent, Example 8, the first paragraph, Lines approximately 16 through 27. This describes a contact lens soak, wouldn't you agree with that, Mr. Dziabo?
A. It's so written.
Q. Included in this contact lens soak is chlorine dioxide. Is that correct, sir?
A. That's correct.
Q. And it states here that, "The known bactericidal,

fungicidal, and viraloidal capacity of chlorine dioxide along with the low toxicity makes chlorine dioxide solution an ideal lens soak."

Is that correct, sir?

A. **Yes.**

Q. **And we are talking about contact lenses. Is that correct, sir?**

A. **Yes.**

Q. **And contact lenses are ultimately placed in the eye. Is that correct, sir?**

A. **Yes.**

Q. **The next sentence says, "In addition, capacity to degrade organic debris keeps the lens clean and non-irritating."**

Is that correct, sir?

A. **Yes.**

Q. **Then, finally, it says, "The preferred range of concentration" -- and I believe this is referring to the chlorine dioxide. Correct, sir?**

A. **That would be my interpretation.**

Q. **So the preferred range of chlorine dioxide is .005 percent to .2 percent in sterilized water. Is that correct, sir?**

A. **Yes.**

Q. **And .005 percent is the same concentration that you**

used?

A. Incorrect.

MR. SODIKOFF: Your Honor, can I have one second?

THE COURT: Yes, sir.

(Pause.)

BY MR. SODIKOFF:

Q. Continuing in the Radcliff patent, if we could look a little broader at just the top half of this, on the bottom, Line 36, it says that chlorine dioxide is approved by the Environmental Protection Agency. And it gives the No. EPA Reg. No. 9048-3.

Are you aware of that EPA regulation number, sir?

A. That's a registration number, not a regulation number.

Q. Do you know that register number, sir?

A. I do not know that registration number.

Q. Do you know that that registration number is for Oxine, which is a Purogene product?

A. It very well could be. I have not memorized all the EPA registration numbers for various products.

Q. Thank you, sir.

Sir, do you still have your book from yesterday?

A. Yes, I believe so.

Q. Do you have JTX-083 in there?

A. **Yes.**
Q. **I believe yesterday you mentioned that you came across, was, I think, the language you used, this document?**
A. **Yes.**
Q. **Wasn't it, in fact, this document sent to Allergan by Bio-Cide along with that March 2nd, 1983, letter?**
A. **I would have no knowledge of that.**
Q. **You have no reason to dispute that, though, do you, sir?**
A. **It's possible.**
Q. **Turning to the second page of this document, at the top -- actually, let's just move on past that.**

Let's go to Page 3, Allergan 730572. Isn't it true that Bio-Cide is describing stabilized chlorine dioxide as a dilutable liquid, and that the solutions display a great deal of application flexibility-adjustments in concentration, pH, and contact time can be made to fit a large array of applications? Is that correct, sir?

A. **That's what it reads.**
Q. **In the next paragraph, it states that "the products have very low toxicity to mammals."**

Isn't that correct, sir?

A. **That's what it states.**
Q. **In fact, the Stockel '077 patent that we looked at put stabilized chlorine dioxide in an eye formulation. Isn't**

that correct, sir?

A. They described the formulation for use in contact lens care.

Q. And that formulation that they described included stabilized chlorine dioxide. Is that correct, sir?

A. That's correct.

Q. So you certainly were not the first person to describe using stabilized chlorine dioxide in an eye formulation, were you, sir?

A. That's correct.

Q. Here, it goes on to say that, "Class 3 chemicals which represent the next to the lowest toxicity."

Is that correct, sir?

A. Yes.

Q. Finally, this last one is pretty interesting, it says, "No special precautions are required, and, in fact, the product is currently registered up to 50 parts per million as a potable water treatment chemical for human consumption."

Is that correct, sir?

A. That is correct.

Q. 50 parts per million is the concentration that you use in your -- that you describe in your patent. Isn't that correct, sir?

A. That's correct.

Q. **If we can move on to Allergan 0730578. This is the biological report that you discussed yesterday. Isn't that correct, sir?**

A. **That's correct.**

Q. **And the ingredients here include chlorine dioxide at two percent. Is that correct?**

A. **That's correct.**

Q. **Isn't that 20,000 parts per million?**

A. **Yes, it is.**

Q. **But on the other page, didn't they say that you could use stabilized chlorine dioxide at 50 parts per million?**

THE COURT: The question is argumentative, counsel. You can make that argument at closing. Let's ask the questions, get the answers and move on.

MR. SODIKOFF: I apologize, Your Honor.

BY MR. SODIKOFF:

Q. **This concentration of 2 percent stabilized chlorine dioxide, 20,000 parts per million, was shown to be only a slight ocular irritant. Isn't that correct?**

A. **In this test, yes.**

Q. **And your concentration is many times less concentrated than here, isn't it, sir?**

A. **That's correct.**

Q. **Mr. Dziabo, I have handed you DTX-359. Is that correct?**

A. **Yes.**

Q. **This is a statement about anthium dioxcide. Is that correct, sir? If you look at "Directions For Use," I think you see the name there a couple times?**

A. **Yes.**

Q. **And anthium dioxcide is an example that you provided in your patent as a stabilized chlorine dioxide. Is that correct, sir?**

A. **Yes.**

Q. **If we can go to Page 3 of this document. I would like to look at the typical properties of this anthium dioxcide.**

A. **Not the third page, but Page 3?**

Q. **I am sorry. It's AI 0026855, Page 3 of the document but I think it's numbered Page 1 on the bottom.**

A. **Yes, that's my confusion.**

Q. **Here, it describes the formulation anthium dioxcide. Is that correct, sir?**

A. **Yes.**

Q. **And it says that anthium dioxcide includes sodium carbonate that's 3.65 percent, and chlorine dioxide, 5 percent. Is that correct, sir?**

A. **Yes.**

Q. **And the other ingredient is water?**

A. **Yes.**

Q. **And the shelf-life of this product exceeds one year.**

Is that correct, sir?

A. **Yes.**

Q. **Mr. Dziabo, I have handed you DTX-253. I would like to ask you, at the top, what this is?**

A. **It's titled, "Patent Specification."**

Q. **And it's a Great Britain application. If you can tell me the -- what years you see described here under the patent specification? Specifically, the complete specification published date.**

A. **24 May '72.**

Q. **And this patent describes, Line 43 in Column 1, "We have now found, surprisingly, that the undesirable microbial growth or contamination in antacid compositions does not incur in the case of an aqueous antacid composition, which comprises water and aluminum hydroxide and/or magnesium trisilicate and/or magnesium hydrocide, together with .005 to .100 percent by weight of chlorine dioxide as a preservative."**

Is that correct, sir?

A. **Yes.**

Q. **And it moves on, in Column 2, Line 60, that chlorine dioxide has been used extensively in water purification processes?**

Is that what it tells us, sir?

A. **Yes.**

Q. **And then it says that, "The activity of this compound is dependent upon the pH."**

Is that correct, sir?

A. **Yes.**

Q. **Then it goes on and gets a patent in 1972 for saying that, "It is quite surprising that, even in a high alkaline pH, such as those systems containing antacid compounds, it is capable of suppressing growth of microorganisms."**

Is that correct, sir?

A. **Yes.**

Q. **If we could look at the next page, Page 885, Line 8 through 13: "Chlorine dioxide in the form of gas is bubbled into the solution, or a solution containing 5 percent by weight chlorine dioxide and 3.65 percent by weight sodium carbonate is added."**

Did I read that correctly, sir?

A. **Yes.**

Q. **Do you recognize those as the exact two concentrations that were found in the anthium dioxcide product?**

A. **Yes.**

Q. **Mr. Dziabo, I think that you looked at DTX-226 yesterday in your booklet. Do you still have that with you?**

A. **DTX-226?**

Q. **Yes, sir.**

A. **Yes.**

Q. **On the second page -- I am sorry, the third page, Bio-Cide 00535 -- actually, I think there are four zeros, but Bio-Cide 535.**

A. **Yes.**

Q. **Everyone here has this page, if we could turn that off, the 5 and 6 are redacted. Is that correct, sir?**

A. **In my copy, yes.**

Q. **In No. 7 -- at the top here, it says November 19, 1986. Is that correct, sir?**

A. **That's correct.**

Q. **If I can put it on the Elmo.**

If we can go back to the first page of this for just one second. It lists here the people who were attending the meeting for Bio-Cide and for Allergan. Is that correct, sir?

A. **Yes.**

Q. **And these are some pretty important people at Bio-Cide, aren't they, sir?**

A. **Yes.**

Q. **We have Mr. Danner, the president, Mr. Knapp, vice president, Mr. 0. Hardy, another vice president, Mr. Ringo, the assistant technical director, and we actually have a Mr. Wilkens, chairman of the board.**

Is that correct, sir?

A. **That's correct.**

Q. **Also, for Allergan, we have Mr., and I will probably murder this, Karageozian, vice president, we have Mr. Kiral, the director, we have you, sir, the manager, we have Mr. Ripley, the senior professional, we have Mr. Courtney, a director, and we have two other managers and two other senior personnel.**

Is that correct, sir?

A. **Yes.**

Q. **And looking at, going to the next page -- Page 3 of this document, Bio-Cide 53. If we look at No. 7 here.**

A. **Yes.**

Q. **It states that, "In order to strengthen the cooperative development efforts between Bio-Cide and Allergan and ensure prompt and necessary communications, Bob Danner proposed a monthly project review which would update all parties on the status of experiments, patents, and other pertinent project issues."**

Is that correct, sir?

A. **That's correct.**

Q. **So Mr. Danner proposed a monthly project review that would include an update to all parties on patents. Is that correct, sir?**

A. **That was an agenda item to be discussed at the meeting.**

Q. **Mr. Dziabo, yesterday, you said that you were not**

aware that Bio-Cide and Allergan filed patent applications on the exact same day. Is that correct, sir?

A. **I was not aware up until the time of my deposition, that's correct.**

Q. **But you are aware of it today, sir?**

A. **Excuse me?**

Q. **Are you aware today?**

A. **Obviously, yes.**

Q. **And you don't dispute that the specifications of those two patent applications are largely exactly the same?**

THE COURT: You might want to establish that he is familiar with the other.

MR. SODIKOFF: Sorry.

BY MR. SODIKOFF:

Q. **Have you had an opportunity to look at the Bio-Cide patent application?**

A. **No, I have not.**

Q. **Mr. Dziabo, if I can just -- Mr. Dziabo, is this a document that you haven't seen before?**

I am sorry.

Can you just tell --

A. **This is one of many documents I have never seen before.**

Q. **The serial number at the top, can you just tell me what that says, sir?**

A. **It's a little difficult to read the serial number.**

Q. **JTX-099, Bio-Cide 615.**

A. **I am not with you here.**

Q. **I was just telling him the Bates number on the back.**

The serial number is on the top.

A. **What I have in the serial number here on the top is AWS, it appears.**

Q. **Under that, sir.**

A. **Under it?**

Q. **Yes.**

A. **This copy is a little weak. It looks like it's better on the screen.**

07/277, 790. That's the best I can read.

Q. **The filing date, sir, next to it?**

A. **I would say 11/29/83.**

Q. **I believe that's an '88, sir.**

A. **It's hard to read.**

Q. **But the first named applicant?**

A. **I am going to guess Danner.**

Q. **If I represented to you that it said Danner, would you recognize that name?**

A. **I would say that's possible.**

Q. **And that is Mr. Bobby Danner from Bio-Cide. Is that correct? Do you know a Mr. Bobby Danner from Bio-Cide?**

A. **It says "Danner."**

Q. **The next part is Bill D. McCarthy. Do you recognize that name, sir?**

A. **I recognize that name, yes.**

Q. **And he was an attorney for you in your patent application. Isn't that correct, sir?**

A. **My recollection of Mr. McCarthy's involvement in the patent application is very weak, over time. I remember Mr. Uxa being the primary person I dealt with.**

Q. **Let me show you JTX-075.**

Do you have JTX-075 in front of you, sir?

A. **Yes, I do.**

Q. **I would like to look at AI 17334.**

MR. SINGER: My copy does not have that.

THE WITNESS: Mine doesn't, either.

MR. SODIKOFF: I apologize.

BY MR. SODIKOFF:

Q. **Do you have AI 17302 up there, sir.**

Do you have that document, sir?

A. **I am sorry. What was the document again?**

Q. **AI 17302.**

A. **Yes.**

Q. **And this is the part of the prosecution history for the original patent that you -- it was a C-I-P and eventually became the '078 patent. Is that correct, sir?**

A. **I believe so.**

Q. **And about halfway down, under, does it list a Mr. Bill McCarthy, Bill D. McCarthy?**

A. **Yes.**

Q. **And name him as your lawyer, sir?**

A. **I don't know what that means. His name is listed there.**

Q. **If we can look at the next page of this document, AI 17334.**

It's not the next page of yours. But AI 17334.

A. **Yes.**

Q. **Do you recognize, at the top, that this says, "Declaration and the Power of Attorney-Original Application"?**

A. **Yes.**

Q. **Do you recognize, about halfway through, that you hereby appoint Bill D. McCarthy to be your attorney?**

A. **Yes.**

Q. **And down below, the full name for sole inventor listing Anthony J. Dziabo, Jr. That is you, sir. Correct?**

A. **Yes.**

Q. **Would you agree with me that in this power of attorney, you made Mr. Bill D. McCarthy your attorney for this patent application?**

A. **It appears so.**

Q. **And if we go back just for a second to JTX-099, the**

first page?
A. JTX-099, okay.
Q. That also lists Mr. Bill D. McCarthy. Is that correct, sir?
A. Yes.
Q. So you would agree with me now that Mr. Bill D. McCarthy filed both of these applications?
A. I don't know if he filed both applications. I have no recollection of that.
Q. He is listed as the attorney on both applications, though. Isn't he, sir?
A. Yes.

MR. SODIKOFF: Thank you, Mr. Dziabo.

THE COURT: Mr. Boggs?

MR. BOGGS: I have no questions, Your Honor.

THE COURT: All right. Your redirect, Mr. Singer.

MR. SINGER: Thank you, Judge. If I may have a moment to get a little organized, then we will go forward.

THE COURT: All right.

REDIRECT EXAMINATION

BY MR. SINGER:

Q. Good morning, Mr. Dziabo. Good to see you again. I want to start with, it was right near the end before we got to the patent applications that you hadn't seen before.

DTX-253, please. Do you still have a copy of that up there? That is this British thing with the seal on the front.

A. **Yes.**

Q. **If I can direct your attention to the paragraph that counsel showed you, which is at the bottom of the first column overlapping to the second.**

A. **Yes.**

Q. **And if we could put that together, to get the whole paragraph, please.**

This is the invention in this patent, is it not?

A. **That's correct.**

Q. **It says, "We have now found," and you have patents. Correct?**

A. **Yes.**

Q. **And this is -- do you understand this to be a way of saying this is what I have invented?**

A. **Yes.**

Q. **And doesn't it say that, "We have now found, surprisingly, that the undesirable microbial growth or contamination in antacid compositions does not occur in the case of an aqueous antacid composition, which comprises water and aluminum hydroxide and/or magnesium trisilicate and/or magnesium hydroxide, together with .005 to .100 percent by weight of chlorine dioxide as a preservative"?**

A. **Correct.**

Q. **Did I read that correctly?**

A. **Yes, sir.**

Q. **That is not stabilized chlorine dioxide. Is that right?**

A. **That's not -- I agree with your interpretation, this is the chlorine dioxide gas, not stabilized chlorine dioxide.**

Q. **Thank you.**

Now I would like to go to -- Mr. Dziabo, you should have the International Dioxide label in front of you.

A. **I am sorry?**

Q. **The International Dioxide label, which should be marked as DTX-359. And I know you probably have a pile of papers up there.**

A. **359, yes, I have it.**

Q. **Counsel walked you through the composition of this product.**

A. **Yes.**

Q. **And that was, I believe at Page 3 of the document, which is Page 1 internally, which is AI -- it's Page 1 internally, Page 3 of the exhibit, which is AI, in very small print, 0026855.**

A. **855.**

Q. **It's the third page of the exhibit.**

We are getting closer.

It should say "typical properties." Do you have that, Mr. Dziabo?

A. **I have the packet.**

MR. SINGER: May I approach, Your Honor, just to help?

THE WITNESS: I can't find 855.

855, I have got it. Those numbers are kind of small.

BY MR. SINGER:

Q. **They are very small.**

That describes chlorine dioxide as the active ingredient, does it not?

A. **Yes, means of using chlorine dioxide in products and processes.**

Q. **And, again, that is the gas, not the stabilized chlorine dioxide. Is that right?**

A. **That's correct.**

Q. **And then if I could even turn to the front page of this document, you will see it says a note on the front, and I will read it, if we can highlight it, can we spin that so we have it, highlight just the note, where it says, "Note," and I will read that: "All working solutions must be adjusted to pH of approximately 4.0 prior to use, employing acidic acid, vinegar, citric acid or suitable buffer, or added to a medium which will result in a final pH of 4.0."**

Did I read that correctly?

A. **Yes, you did.**

Q. **That will result in the production of chlorine dioxide gas, will it not?**

A. **That's correct.**

Q. **You can put that aside.**

Mr. Dziabo, if you can go to JTX-83. This is the packet of material that you said you reviewed?

A. **Yes, I am there.**

Q. **Do you recall being asked by counsel about the use of -- I think he said stabilized chlorine dioxide in water treatment. Do you remember that?**

A. **Yes.**

Q. **I would ask you to turn to the Bates stamp page Allergan 0730577. And I would like to highlight Section 3. That describes the "use of chlorine dioxide in water treatment," does it not?**

A. **That's correct.**

Q. **Again, that's the gas. Right?**

A. **That's correct, chlorine dioxide is the gas.**

Q. **That's not the stabilized chlorine dioxide, which is the sodium chloride we talked about yesterday. Right?**

A. **That's correct.**

Q. **I think you can put that aside.**

If we can have, I think counsel showed you

DTX-118.

A. **Is that in the book?**

Q. **No. It was handed to you by counsel. It's the Radcliff '214 patent.**

A. **Yes.**

Q. **And he referred you to the example of the contact lens soak, which is Example 8 on Columns 11 and 12.**

If we could highlight the first paragraph, and it's really the second sentence, it says, "The known bactericidal, fungicidal and viraloidal capacity of chlorine dioxide along with the low toxicity makes chlorine dioxide solution an ideal lens soak."

I don't mean to be repetitive. But, again, is that chlorine dioxide, the gas?

A. **That's how I would read this sentence.**

Q. **And then, again, if we go to the bottom of Example 8, it's the last sentence, and it says, "Chlorine dioxide is approved by the Environmental Protection Agency, (EPA Registration No. 9048-3), for water purification, food preparation and preservation as well as a bacteriostatic, fungistatic and virostatic agent."**

Did I read that correctly?

A. **Yes.**

Q. **And again, that's the gas, not the stabilized chlorine dioxide. Right?**

A. **Yes.**

Q. **You can put that aside.**

I think -- you had a discussion with counsel about some arguments your -- one of your lawyers made, Mr. Uxa, do you recall that? It was right at the outset of your activity?

A. **Yes.**

Q. **He kept claiming that your lawyer had admitted that chlorine dioxide -- or stabilized chlorine dioxide is a well-known preservative. Do you remember that?**

A. **Yes.**

Q. **If we could bring up the brief, and I would like to show you something that he didn't tell you. If we could go to Allergan, I think it's JTX-006B.**

Do we have that, Mr. Exline?

A. **JTX-?**

Q. **006B. Mr. Dziabo, it is one of these briefs that we lawyers file?**

A. **It's in my book?**

MR. SINGER: May I approach to help, Your Honor?

THE COURT: Yes. I think it was handed to you.

THE WITNESS: I have it. Oh, it was 063?

MR. SINGER: Let me approach, Your Honor.

BY MR. SINGER:

Q. **Now, I am going to read from Allergan 978398. It is**

down near the bottom of the page.

I think counsel showed you the paragraph that says "the fact that."

Do you see that? Do you remember him showing you that?

A. **Yes.**

Q. **He didn't show you the preceding paragraph, did he? And I will highlight the preceding paragraph.**

If we can just have the preceding paragraph.

"The Examiner contends that stabilized chlorine dioxide is well-known as a preservative in many applications and that it would be obvious to adapt it to ocular applications."

So that was the examiner's contention in this brief. Isn't that right?

A. **Yes.**

Q. **And your lawyer was responding to the examiner's contention, wasn't he?**

A. **Yes.**

Q. **As you understand it?**

A. **Yes.**

Q. **You were also shown, I think, the -- let's get something on the record here. You were shown DTX-357, which is an FDA, I guess a monograph for over-the-counter products. Do you remember that?**

A. **Yes, I have it here.**

Q. **This is where we went through the requirements for eyewashes?**

A. **Yes.**

Q. **Mr. Dziabo, are you claiming you invented the concept of preserved eyewashes?**

A. **No.**

Q. **Are you claiming you invented the concept of preserved saline?**

A. **No.**

Q. **Thank you.**

THE COURT: Mr. Dziabo, go back to Page 15, if you would, JTX-006B.

Mr. Singer directed you to the first paragraph on that page. Would you read to yourself the first three sentences of the second paragraph and tell me how you interpret it.

THE WITNESS: Page 15, Your Honor?

THE COURT: The paragraph beginning with the word "further." Read those to yourself, those first three sentences, please, and tell me how you interpret that.

(Pause.)

THE COURT: What is the lawyer saying there?

THE WITNESS: Well, he is basically saying that, it reads that the stabilized chlorine dioxide is in

combination with another antimicrobial agent, both of which are necessary to provide the antimicrobial activity for their described invention.

THE COURT: Then the last sentence, he offers the view that, In this important regard, Stockel, et al. patents teach clearly, directly and expressly, away from the present invention. What do you interpret that to mean? Just what it says, I would imagine.

THE WITNESS: I would interpret that as saying that it was an improper interpretation by the reviewer.

MR. SINGER: Thank you, Your Honor. You anticipated where I was going. I was going to put up the Stockel patent.

BY MR. SINGER:

Q. **Just for the record, let's put up the '077 patent, which was DTX-252, Mr. Dziabo.**

A. **Yes, I have it.**

Q. **I will show you a few things that counsel didn't show you, which were the source of the arguments made by your lawyer that His Honor just went through.**

If we could go, just highlight the first line of the abstract. The first two lines, really. It says, "An antimicrobial composition is provided comprising an aqueous solution of an oxyhalogen compound and a polymeric germicide."

The next line says, "The oxyhalogen compound is preferably stabilized chlorine dioxide and the polymeric germicide is preferably a quaternary ammonium compound." Did I read that accurately?

A. **That's correct.**

Q. **And the quaternary ammonium compound is another preservative agent. Is that correct?**

A. **Yes.**

Q. **The oxyhalogen composition was the stabilized chlorine dioxide?**

A. **That's correct.**

Q. **And that is what your lawyer was talking about, and Your Honor just referred you, where the Stockel requires two active agents for preservation?**

A. **That's what it describes to me.**

Q. **Also, you were referred to, I believe, Example 2. It was the sentence that he read, I think, that said, it's Column 12, if I can help, Additional Example 2. I think counsel read to you -- actually, he didn't read this to you, now that I think about it.**

It says, "The antimicrobial effectiveness of the combination of IL-779 and stabilized chlorine dioxide was measured by a broth dilution method."

Did I read that correctly?

A. **Yes, you have.**

Q. **Again, the stabilized chlorine dioxide was not a sole preservation in this composition. Correct?**

A. **It was not the sole antimicrobial agent in this composition.**

Q. **What is your understanding of how the stabilized chlorine dioxide was used in Stockel's inventions?**

A. **Stockel describes an invention where the stabilized chlorine dioxide is used as what is known as a potentiator.**

Q. **What does that mean?**

A. **Basically, a potentiator is a substance that interacts with another substance in a manner to enhance or to leverage or to increase the desired functional effects.**

Q. **So, if I understand this correctly, the stabilized chlorine dioxide was used to sort of activate the other preservative to make it more effective. Is that right?**

A. **That's correct, yes.**

Q. **Actually, let's go to Column 11. It was the table right there, at the bottom, and I remember counsel going through that. Do you remember him going through that?**

A. **Yes.**

Q. **Do you remember when he skipped the polydiguanide?**

A. **Yes.**

Q. **Mr. Dziabo, I would ask you to look at DTX-216. This was the letter that you were shown?**

A. **So it's in the book?**

Q. **No. It's something that counsel handed you. It's a one-page letter.**

A. **I have it.**

Q. **I am sorry.**

MR. SINGER: Your Honor, before I do that, I would actually like to show the witness the appeal, if I could.

THE COURT: Yes.

MR. SINGER: Your Honor, it's an excerpt from DTX-257. I have excerpted it to make things easier. It's the file history. I just took a piece from it.

BY MR. SINGER:

Q. **I would ask you to look at Page 4, Mr. Dziabo. This is the appeal that counsel referred you to in the Patent Office.**

You understand it took place in the Patent Office?

A. **Yes.**

Q. **I didn't mean to suggest yesterday it had taken place in an appellate court. It was the Patent Office.**

You understand these to be the findings on appeal?

A. **Yes.**

MR. SODIKOFF: I object, Your Honor. The decision by the board, the appeal, the brief, I think it

speaks for itself. Mr. Dziabo certainly didn't write it.

THE COURT: Overruled.

BY MR. SINGER:

Q. **If we could turn to Page 4 of the board's decision.**

A. **I am on Page 4, yes.**

Q. **I can also put it on the Elmo.**

THE COURT: He didn't write the lawyer's briefs, either, counsel.

BY MR. SINGER:

Q. **I am going to switch to the Elmo. Okay.**

Right here. I will read this from the board's appeal, that, "such positively charged nitrogen-containing cationic polymers are critical to Stockel's invention is clear from the disclosure of the Stockel '208 patent, Column 9, Lines 5 to 13 reproduced below."

Did I read that correctly?

A. **Yes.**

Q. **That is consistent with your understanding of the Stockel patents?**

A. **Yes.**

Q. **It is not just the Stockel '208 patent but the other Stockel patent you were shown?**

A. **Yes, it is.**

Q. **Now I would just like to refer you to the letter again, which is Defendant's Exhibit 216.**

Mr. Dziabo, you were going to say something about the line there about the preservative thimerisol. You were told it was a yes or no question.

What is it that you wanted to say about that?

A. **I just wanted to make the point that I thought that the terminology of the preservative was very loose, and that the more correct indication in my interpretation, there should have been the antimicrobial agent thimerisol, because, in reading this letter, we did have a disinfectant product called Allergan Hydrocare Cleaning and Disinfecting Solution. It was a soft lens disinfecting solution.**

And it used the quaternium and the thimerisol in combination, they were the two -- they were, the two were together. It is the only product where we had a combination of thimerisol and quaternium.

So he had to have been looking at and referring to the disinfecting product, so his terminology of preservative in this instance was incorrect.

Q. **Thank you.**

MR. SINGER: I have nothing further, Your Honor.

THE COURT: All right. You are excused.

MR. SODIKOFF: Your Honor, may we just have a moment?

THE COURT: No, that is it. I explained my process. You can ask, or if I offer it, okay.

(Witness excused.)

THE COURT: I think we will take our morning break.

(Recess taken.)

THE COURT: All right. Please take your seats. Ms. Brooks, you were about to say?

MS. BROOKS: Yes, Your Honor. Allergan calls its next witness, Dr. Valentino Stella. Just for context, Your Honor, Dr. Stella, at this point in time, will only be talking about infringement as far as Exela and the '834 patent is concerned. We will be recalling him later after Exela and Apotex have presented their validity case in rebuttal of that case.

Mr. Singer will be doing the direct.

MR. BREISBLATT: With that in mind, I have let some of my team leave, Your Honor.

THE COURT: That is fine.

...VALENTINO JOHN STELLA, having been duly sworn as a witness, was examined and testified as follows...

DIRECT EXAMINATION

BY MR. SINGER:

Q. **Good morning, Dr. Stella.**

MR. SINGER: Your Honor, may I approach to hand the witness his binder?

THE COURT: Please do, Mr. Singer.

BY MR. SINGER:

Q. Good morning, Dr. Stella.

A. Good morning.

Q. Thank you for coming today.

Where are you currently employed?

A. I am currently a distinguished professor of pharmaceutical chemistry at the University of Kansas.

Q. And what is a distinguished professor at the University of Kansas?

A. As you know, the normal ranks of professor is assistant, associate, and full professor. And "distinguished professor" is a higher distinction. It comprises about 40 to 50 professors at the University of Kansas.

Q. What types of courses do you teach?

A. I currently teach classes in pharmacokinetics. Your Honor, that is a time profile of drugs in the body. How drugs are absorbed. How they are eliminated.

I also teach a class in drug stability. And, over the years, I have taught classes in drug formulation, solubility, pharmaceutical equilibrium.

Q. How long have you been at the University of Kansas?

A. This is my 36th year at the University of Kansas.

Q. And when did you become a full professor?

A. I became a full professor in 1981. And a

distinguished professor in 1990, I believe.

Q. **Have you held other positions at Kansas University other than in the professorial capacity?**

A. **Yes, I have had two other positions. From 1989 to 1999, I was the director of the Center for Drug Delivery Research at the University of Kansas. And about three or four years ago, I became director of the Drug Development and Experimental Therapeutics Group within the University of Kansas Cancer Center.**

Q. **You have an Australian accent. Are you from Australia?**

A. **I am, sir.**

Q. **Can you describe your educational background for the Court?**

A. **I have a Bachelor of pharmacy degree which I received in 1968 from the Victoria College of Pharmacy in Melbourne, Australia. Subsequent to that, I worked as a pharmacist for one year in hospital pharmacy.**

In 1968, late '68, I went to graduate school at the University of Kansas, with the late Professor Takeru Higuchi, and received my Ph.D. in 1971.

Q. **What was the subject matter of your Ph.D. thesis?**

A. **It was on the drug delivery and formulation of the antiseizure drug Dilantin.**

Q. **How long have you worked in drug formulations?**

A. **All my career.**

Q. **Do you have any particular experience with ophthalmic drug formulations?**

A. **I have -- yes, I do. When I was a pharmacist at Bendigo Base Hospital, it is a small town in North Central Victoria, I produced ophthalmic formulations. There was no research involved. It was simply batch making of formulations, sterilization, et cetera.**

I then, in my capacity as a consultant to the pharmaceutical industry of 36 years, I have worked very closely with formulators and researchers in the area. And in my own work, I have published a number of papers in the area of ophthalmics, and, also, but much more extensively, sterile products, which have a lot of similarities to ophthalmic formulations.

Q. **Have you consulted for Allergan in the past?**

A. **I have.**

Q. **Have you consulted for other pharmaceutical companies?**

A. **Just about all of them.**

Q. **Have you consulted for generic pharmaceutical companies?**

A. **Yes, I have.**

Q. **Do you have any patents?**

A. **U.S. patents, I think it's 35 or 36.**

Q. **Have you worked on any notable products you would like**

to tell the Court about?

A. I am the inventor or co-inventor of the drug called fosphenytoin, it is also Cerebyx, it is a safe injectable form of the drug Dilantin.

I was also the, I helped formulate the anticancer drug Velcade, which is a new anticancer drug, it's generic name is bortezamib.

I am the coinventor of the top-selling anti-AIDS drug, which is Viread.

I think, Your Honor, you know the product that came out about two years ago, which was three drugs in one tablet, you take one tablet once a day for the treatment of AIDS. The principal drug in that is Viread. I was the co-inventor of that.

Last December, I had the honor of having a new anesthetic drug that went onto the market called Lusedra. There is a product called Captisol, which is a cyclodextrin, it is a safe injectable form of cyclodextrin. That is in five commercially approved FDA products.

Q. Have you served as an expert in patent litigation before?

A. Yes, I have, for both branded names as well as for generics.

Q. Dr. Stella, were you retained to render an opinion on infringement with respect to the Exela defendant here today?

A. **Yes. I was asked by Allergan to be, to offer an opinion as to whether the asserted claims of the '834 patent are infringed by the Exela formulation.**

Q. **Did you reach such an opinion?**

A. **Yes, I did.**

Q. **What is your opinion?**

A. **My opinion is that they do infringe on the patent.**

Q. **You are going to get a chance to come back on validity and talk about a lot of things. But I want to focus you here, because we are only talking about infringement, were there particular aspects of ophthalmic formulation in the area of pH that were important to your opinion on infringement?**

A. **Yes. It is my understanding that that is the major issue that is in dispute here.**

So I will render an opinion on pH as it affects -- pH is an important component of a formulation. It affects solubility, stability, and stability not only of the drug but also of any component that is present in the formulation.

Q. **What is the concept of pH drift?**

A. **PH drift occurs when you have a goal to achieve a particular formulation, either during manufacture and other stages of the product life. And pH of a formulation can drift, depending on the formulation itself.**

That can come from things such as the drug degrading or a component degrading. It can come from the fact that, in the case of ophthalmic formulations, it is a plastic container, not a hermetically sealed container. So you can have absorption of carbon dioxide.

There is a certain amount of evaporation that occurs with ophthalmic formulations on storage. Again, because of the plastic container.

So the pH can drift. It is something that you set specifications on in formulating your drug.

Q. **In reaching your opinion on infringement, what did you consider with respect to that opinion?**

A. **I considered a lot of documents, microorganisms of which are present here. But, largely, it is the '834 patent, itself, both the claims and specifications.**

I also considered the ANDA that was filed by Exela. Communications between Exela and the FDA. Depositions by a number of people that were deposed, Professor Mitra, Dr. Koneru, Stoelzle and Friedly, I believe.

Q. **Is that Friedly?**

A. **Friedly.**

Q. **Were there also additional documents that were produced in the case that you looked at?**

A. **Yes. There was some stability data from India, and I**

believe that's the major documents. I may have missed one.

Q. **We are going to try something a little different. We have a PowerPoint that combines the demonstratives and excerpts from documents in the record.**

We have it on the screen. I will go to the first slide.

Do you understand it to be Claim 1 of the '834 patent?

A. **Yes, that is highlighted, Claim 1 of the '834 patent.**

Q. **Do you understand that in order for there to be infringement, there has to be something that meets each limitation of the claims?**

A. **Yes. The claims are broken down into elements, and it is my understanding that to infringe, it has to infringe on all elements of the claim.**

Q. **We will go to the next slide. Does that break out the elements of the '834 patent, Claim 1?**

A. **Yes, it does. It is a nice way to summarize it.**

Q. **What is the first element?**

A. **The first element is it has to be therapeutically effective aqueous composition, ophthalmic composition comprising, et cetera.**

Q. **What is the second element?**

A. **Up to about .15 percent of bromo-6, et cetera.**

Your Honor, if you don't mind, can I call that

brimonidine?

THE COURT: Please do.

THE WITNESS: Thank you. And a composition having a pH of 7.0 or greater.

And the final element is brimonidine being soluble in the composition at about 21 degrees centigrade.

BY MR. SINGER:

Q. **Let's talk about the first element, the therapeutically effective element.**

What did you review to see whether or not the Exela ANDA met that requirement?

A. **Well, very simply, the fact that Exela filed an ANDA for a generic, to be considered a generic equivalent to the Alphagan P product .15, by that very act of doing that, they are, in fact, telling us that they believe that it is, in fact, therapeutically effective.**

Q. **Now, the FDA ultimately decides whether that is the case. Is that right?**

A. **That is correct.**

Q. **Now, did Exela say anywhere in the ANDA that you saw that they were selling or were attempting to sell a therapeutically effective formulation?**

A. **Yes. In fact, this is a part of the ANDA. I will just read out the document, the part that is highlighted, "Brimonidine tartrate ophthalmic solution is indicated for**

the lowering of intraocular pressure in patients with open-angle glaucoma or ocular hypertension."

Q. **This is, at the bottom, an excerpt from Plaintiff's Exhibit 288.**

A. **That's correct.**

Q. **And that is the Exela ANDA?**

A. **That's correct.**

Q. **It looks like it's a comparison of the generic and reference drug?**

A. **That is correct. They are effectively asking the FDA to approve their product and asking for a bioequivalency waiver to have this product approved.**

Q. **Do you understand there to be a dispute over this limitation?**

A. **No, not to my understanding.**

Q. **Let's go to the next limitation in the claim.**

So we have checked off the first one. The next one is the brimonidine tartrate. Correct?

A. **That's correct, .15 percent.**

Q. **We will go to the exact same document we were looking at before.**

What does it say here from the Exela ANDA?

A. **The Exela ANDA states that the formulation contains, is a solution, and it contains .15 percent. We have cut off the fact that it is brimonidine tartrate. That is at the**

top of that column.

Q. **Does that meet the second limitation of the claim?**

A. **It does. There is also an error in this slide, if you will notice -- not on the slide, but in the ANDA, they said it's a .1 percent, the top column, it should be .15, I assume.**

Q. **Is that the error you are referring to (indicating)?**

A. **Yes. In both columns, both for the Alphagan P as well for the brimonidine solution (indicating).**

Q. **We can see below that they are actually using Alphagan P.15. Right?**

A. **That's correct. I assumed it was just a typographical error.**

Q. **All right. We can check off that box.**

I am going to skip ahead to the fourth element.

By the way, do you understand there to be a dispute about whether the Exela product meets that second element of .15?

A. **Not to my understanding.**

Q. **Let's skip the one where there is the dispute so we can get to that and go to the last element of the claim, the brimonidine tartrate being soluble in about, in the composition at about 21 degrees Centigrade.**

I point you again to that same document.

What does the document say about whether or not

the Exela product is soluble in the composition at the noted temperature.

A. **This slide shows that they claim it to be a solution. So, by a "solution," it means that the drug is soluble in their formulation.**

Also, I think it's on the next slide, they have a temperature range which is on the label, a proposed package insert, I guess, that the product is to be stored at 15 to 25 degrees. In the first claim of the patent, they claim a room temperature of 21 degrees. That is in the middle of this temperature range.

Q. **Does that meet the limitations of the fourth element of the claim?**

A. **Yes. And I don't believe there is any dispute on that.**

Q. **Okay. You do understand there is a dispute about the third limitation. Right?**

A. **Yes, that is my understanding.**

Q. **Dr. Stella, what is your understanding of the pH of Exela's product?**

A. **I wish I knew. If you read the ANDA, an ANDA claim, I think, is stating a, I believe there is a manufacturing pH, a release pH, and a pH range for the lifetime of the product.**

Q. **What is that range?**

A. **The lifetime of the product, I believe, was claimed to be 5.5 to 6.7.**

Q. **Did you have a reaction when you learned that that was the range they were claiming?**

A. **Well, my reaction when I saw that is, No way is the FDA going to approve this product as being bioequivalent to the Alphagan P without clinical trials to prove that to be the case.**

Q. **Did you see anything that confirmed the skepticism?**

A. **Well, the FDA sent them a letter, saying that there was a deficiency, I think that's the term, a deficiency, because the FDA felt that the relationship between pH and effectiveness of the Alphagan P product had been established, and that, therefore, the fact that this product could drift down to a pH as low as 5.5 merely brought into question whether this product could meet that bioequivalency.**

Q. **Let me show you the next slide. Is this that letter that you are referring to?**

A. **Yes, it is. I would like to read it out. "There is evidence that pH and/or Purite preservative plays a role in the ocular bioavailability of brimonidine. Higher pH in the presence of Purite has been reported to increase the bioavailability of brimonidine in the aqueous humor in rabbits. The current reference listed drug, RLD, product,**

Alphagan P .15 percent, with Purite as a preservative, has a pH range of 6.6 to 7.4, whereas, the test product, with benzalkonium chloride, BAK, as a preservative, has a pH range of 5.5 to 6.7. You have not shown conclusively that the difference in pH range between the test and RLD products has no significant impact on bioavailability or efficacy of the drug."

Q. **And, for the record, that is Plaintiff's Exhibit 29 and XLA 000395. It refers to the pH range 5.5 to 6.7?**

A. **That is correct.**

Q. **What is that?**

A. **I think -- this seems to be a moving target. But that was the pH that was claimed as the lifetime pH of the product in the ANDA.**

Q. **Did you see a response by Exela to this letter?**

A. **Yes, I did. As a result of getting this, and I believe it's in the next slide, there was an excerpt from a paragraph in the letter from the FDA to Exela. I have got two areas highlighted there. I would like to just read those.**

Q. **Let me read the exhibit into the record. This is an excerpt from Plaintiff's Exhibit 30 at XLA-000401.**

Dr. Stella, you may go ahead and read what you wanted to.

A. **"The pH range of Exela's proposed product, as required**

by the release specification in ANDA, is 6.5 to 6.7."

That is another moving target. The ANDA release specification is not 6.5 to 6.7.

Q. **What is the release specification in the ANDA?**

A. **The release specification, as best as I can determine, it was 6.2 to 6.7.**

Q. **So this is something different than the release specification?**

A. **It is.**

The last sentence that I have highlighted there is, "Exela plans to submit an amendment to its ANDA within the next few days to clarify the proposed labeling to align with the release specification."

Then again, that's confusing because I am not sure if they are claiming that the 6.5 to 6.7 is the release or the whole lifetime. I am assuming it's the lifetime, because there is a paragraph in the previous page that says that it's, it may be the whole specification.

Q. **And did they, in fact, change the lower limit to a point you could see? They underlined the 6.5 and the 5.5. What was the 5.5 in the ANDA?**

A. **The 5.5 in the ANDA was, as far as I can gather, the lowest pH on the lifetime of the product.**

Q. **Then they change it to a 6.5 here?**

MR. BOGGS: Objection. There was no change made

here, Your Honor. It is mischaracterizing what that letter is talking about.

MR. SINGER: Your Honor, that sounds like cross-examination.

THE COURT: Yes, Mr. Boggs. No. 1, you can't testify. You can certainly examine the witness about that on cross.

The objection is overruled.

BY MR. SINGER:

Q. The proposed change is to change the 5.5 to a 6.5. Is that correct?

A. That was my interpretation, yes.

Q. Is that significant, in your view?

A. That is very significant, because, as we will see in some stability data, pH drift data that is in both the ANDA and in some additional data, my feeling is that you cannot maintain a pH of 6.5 to 6.7 without producing a product that would be up into the pH range that infringes on the about 7.0 element of Claim 1 and other claims.

Q. Let's just get some terminology straight, because I think it will help. What does it mean for the product to have a release specification? What is that?

A. There is usually -- the release specification is when the product leaves the manufacturer and is available to the public to be used as a prescription, yes.

Q. **Is that different from the manufacturing pH?**

A. **Yes. The manufacturing pH is usually a pH in which, literally, the product is manufactured at. That manufacturing pH may be different than the release pH, if there has been some pH drift. It usually takes two to three months from manufacture to where it is on the shelf to that, quote-unquote, the release condition.**

Then there is a third element, or the third aspect of pH. That is the lifetime of the product over two years.

Q. **Now, we have the 5.5 to 6.7 range. That reflects a downward drift in the pH. Is that correct?**

A. **Yes, it does.**

Q. **In a product with a downward drift in the pH, is the manufacturing pH going to be above the release pH?**

A. **It isn't necessarily for all products. But, clearly, in this case, based on the ANDA data, the ANDA stability data, and other data that has been presented, that we will be presenting, Your Honor, there is a very significant drift in pH with this product.**

In fact, even over a relatively limited period of time, pH drifts of up to half a pH unit were observed.

Q. **Let's take a look at some of that data?**

One other question: Did you also see that your -- was there someone else who agreed with your

assessment -- let's move on.

Let's take a look at the actual data.

Dr. Stella, I have gone forward two slides. What are we looking at here? It's Plaintiff's Exhibit 35 at EX-022333.

A. **Yes. This was called Long-Term Stability Data.**

Your Honor, there is two types of stability work that is usually done. One is what we call long-term stability. It is really essentially storing the product under the same conditions as the product is expected to be stored, for example, in a pharmacy, on average, in a home.

Usually, you do that study over an extended period of time. Often, you want to confirm at the end of the study that the drug, or the product, in fact, you can put the label on, Use by December 2010.

When you pick up your prescription and the prescription says, or the bottle says, Use by 2010, that is the shelf life of the product.

So long-term stability is where you put the products up under conditions that would be considered to be an average, if you like, for room temperature.

You can see here that this is data taken from a 15 mil bottle. It was stored at 25 degrees and 60 percent relative humidity. This particular product was stored in an inverted condition.

Q. **What does that mean, Dr. Stella?**

A. **If you ever used eyedrops, Your Honor, it's a plastic bottle, it is a dropper bottle.**

When you normally would store that on your, hopefully not in your bathroom, with the high humidity, but if you store that product, you would normally leave it in its normal vertical condition.

But if you were to take that into your briefcase, et cetera, it could, in fact, become invertible, lay on its side.

So the inverted condition is, you are required, in ophthalmic process, to study the stability of the product, both in the normal vertical position as well as in an inverted position.

What you can see here is that they had an initial pH of 6.7, and after three months of storage, the pH had dropped down to 6.2. Then, for some reason, it went back up to 6.4. I have no idea why that happened.

Q. **Did you also review other long-term stability data?**

A. **Yes. I think that's shown on the next slide.**

Q. **I think we have a demonstrative on the next slide which is a graph of this stability data.**

A. **Yes. There was a number of pages of this. Just for ease of clarification, I will just graph them. It is a little easier for us to read what those numbers mean.**

Q. **Let's go through the graph. This is ADX-26.**

We looked at the 15 milliliter fill, the prior page. Right?

A. **Right.**

Q. **That's the orange line. We used, for some reason, various shades of yellow and orange. I suppose we should have chosen different. But what is the yellow line that we are looking at?**

A. **The yellow line is for ten mil fill. There were, apparently, three bottle sizes that were planned, a 5 mil, 10 mil, and 15 mil fill. I drew the red line at pH 6.5, because that is the questionable, whether it is released product. I am not going to -- when Mr. Boggs presented his opening, he showed a range of pH's that were different than what I interpreted the pH to be. But we drew the line at 6.5 regardless of how you interpret that.**

What it shows is under long-term storage, there was at least a drop of greater than .2 of a pH and as high as .5 of a pH, Your Honor. That is the antilog, Your Honor. The antilog of pH, of .5, actually, is a threefold difference in change of fraction of drug in the unionized forms. What you can see, regardless, is a very rapid dropoff of pH.

Q. **Did you also look at the, quote, accelerated pH stability data?**

A. **Yes, I did. Can I explain to Your Honor what accelerated studies represent? I think one of the previous witnesses described it to you. And I think did a very nice job.**

But the accelerated stability study is, you don't want to develop a formulation, wait two years to see if it works, and then find out it didn't work and you have lost two years.

What we do is do accelerated stability testing. That means we expose the product to elevated temperature conditions, and exposing it to elevated temperature conditions, we push any changes along.

There are what's called ICH, it is a harmonization guideline around the world, that says that you aim to, in fact, look at to get at lease adequate stability at 40 degrees, that is 15 degrees higher than 25 degrees, and you look for whether your product is within specifications over three months.

That is often projected, not always accurately, but often projected to be able to say that you will get a -- you have got a greater chance of having a shelf life stable product over two years.

Q. **Let's go to the next slide. Is that some accelerated pH stability data from the ANDA?**

A. **Yes. This is a stability data for the ANDA, Your**

Honor. You will notice that the test condition there says 40 degrees at 75 percent relative humidity. That is the ICH guidelines.

You can see that at zero time they have a pH of 6.7. And within one month, the pH had drifted down to 6.2. And within two months, it drifted down to 6.2.

Q. This is from PTX-288 at EX-003380?

A. That's correct.

Q. By the way, just for the record, this is not data that Exela generated. Is that right?

A. No. This was actually done by Pharmaforce.

Q. Who is Pharmaforce?

A. Again --

Q. To your understanding?

A. It is my understanding that they, that Pharmaforce acted as the U.S. agent for applying to the FDA for Exela, and that these stability studies, I think, were performed by Pharmaforce.

Q. Is most of the data in the ANDA from Pharmaforce?

A. I believe all the data in the ANDA is from Pharmaforce.

Q. And then we have, further -- by the way, what does the accelerated pH stability data show?

A. What it shows is that there is a drift of, over two months, of about .5 of a pH.

Q. **I think we have, further, accelerated pH stability from the next slide. What is this we are looking at, Dr. Stella?**

A. **This is another, also done at 40 degrees upright. I think the previous one was inverted. This one is upright. Again, over three months in this case. We don't have a two-month, one- or two-month study. But, again, we got about half a pH in the drift, from 6.7 to 6.2.**

Q. **This is for the record PTX-288 at EX-003331.**

Then we go to the next slide, which I believe is a demonstrative that you prepared?

A. **It is a graph of the same data that we just talked about.**

Q. **What is the dashed line at 6.5, what does that reflect?**

A. **Again, it reflects both the change from 6.7 to 6.5. What it shows is that if someone was to have a release pH of, for example, 6.7, and from manufacture to release, which is two to three months, there could be up to .5 of the pH unit drift during that time.**

When I say that the product infringes, it would seem difficult to me, if not impossible, for Exela to produce a formulation with a pH of 6.7 on release, that could not be that as manufactured at a pH that begins to directly infringe into the about 7.0 claim of the patent --

element of the patent.

Q. **Let's do the math and we will make it simpler. 6.7 plus .5 is 7.2?**

A. **Yes.**

Q. **And 6.5 plus .5 is 7.0?**

A. **7.0.**

Q. **And both of those about 7.0 or are greater?**

A. **That's correct.**

Q. **Besides the stability data, from the ANDA, did you also look at stability data that Exela had prepared before filing the ANDA?**

A. **Yes. There is two additional pieces of information that I would like to talk about on pH. The first is some stability data that apparently was produced by Exela, it was not in the ANDA, but came up during discovery, I assume.**

Q. **Let's go forward to that, and we have the next slide, which is PTX-208 at XLA-004358. It also comments on PTX-209 and PTX-123.**

What are we looking at here?

A. **This is data I assume generated by Exela in India. It's interesting that they, I believe they state that the target initial pH was 6.9, but they actually made a solution of pH 7.08 as the initial pH. There is two pieces of data there. There is both the 25 degree data at 60 percent relative humidity and the 40 degree data. It is all in the**

same table in this case, Your Honor.

You can see that the initial pH for both samples was started off at 7.08. And, as you can see, both in the 25-degree data as well as with the 40-degree data, there was a substantial drift in the pH with time in the range of approximately .3 to .5 pH units?

Q. If we just see the circles that you have made, 7.08 minus 6.09 is just about .5?

A. .5.

Q. Did you also draft the stability data from Exela India?

A. Yes, I did.

Q. ADX-28. That is the next slide. What are we looking at here?

A. This is just data plotted on the graph for visual purposes. This formulation, assuming it was manufactured, the pH, as so stated, would have infringed if --

Q. If made at that pH?

A. Made at that pH. You can again see the drift of approximately .5 pH units in the 40-degree data over three months and approximately .3, .4 of a pH unit at 25 degrees over three months.

Q. We have highlighted, again, this time at the bottom of the chart, the 6.5. What does that reflect?

A. That reflects whatever their pH means in their

formulation. Again, it appears to be a moving target. To, in fact, keep the pH above 6.5, they would have had to manufacture the product at pH of approximately 6.7 to 7.1.

Q. Dr. Stella, did you also look at any other data surrounding the pH of the proposed Exela product?

A. Yes, I did.

There was a bioavailability study performed by Professor Mitra in five rabbits. That was done as evidence to supply to the FDA, part of the ANDA, that they felt that their .15 percent solution was bioequivalent to the Alphagan P product.

Q. And what was the purpose of submitting this study to the FDA?

A. The purpose of the study was an intent to get a waiver that would allow them to claim that their product was bioequivalent to the Alphagan P .15 percent solution.

Q. What are the consequences of the FDA granting a waiver, if you know?

A. Well, it would allow them to, in fact, go on the market and compete with the Alphagan P product.

Q. Does it also mean they don't have to run clinical trials?

A. Yes.

Q. Let's look at that. Just one more question for the record. Was that rabbit study included with the Exela ANDA

at the FDA?

A. **Yes, it was. But there was a piece of evidence that was, in fact, not supplied to the FDA.**

Q. **Let's look at that.**

This is an excerpt from PTX-288, the Exela ANDA, at DXE-000047.

What does this say in Exela's request for a bioequivalence waiver?

A. **Basically, on the first block, there is a lot number. That lot number represents a production lot number of some kind. I assume it was a lot number produced by Exela.**

And they then state in a subsequent paragraph, "However, because both the Exela product and the Alphagan P product were studied under same conditions, Professor Mitra states that he had statistically indistinguishable IOP lowering from the two products in question."

Q. **So this was -- was this a study in rabbits?**

A. **It was done in rabbits. It was five rabbits.**

Q. **It compared Alphagan P to supposedly the Exela proposed product?**

A. **That's correct.**

Q. **Was the pH of the formula 05 BT 0S09A contained in the request for bioequivalence waiver that Exela supplied to the FDA?**

A. **Exela did not, or Pharmaforce, the combined entities,**

did not, to the best of my knowledge, tell the FDA what the pH of the solution was.

Q. Did you learn what the pH of that solution was during discovery in this case?

A. Yes. There was a document, I think it was a document, I assume, from Professor Mitra to Exela executives, a report, if you like, of their formulation and their findings.

Q. What was the pH that they failed to report to the FDA?

A. The pH that they did not give to the FDA was pH 6.9. In my opinion, the 6.9 is a pH that one infringes on the patent, that is, that it is about 7.0.

In addition, the performance of this drug product is well within the scope of the Alphagan P product, it is potentially a higher pH, has a higher probability of being bioequivalent, not the pH below 6.7.

Q. Let's take a look at the documents you relied on for the pH 6.9. What are we looking at here Dr. Stella? It is PTX-014 and XLA-0002518.

A. If I remember correctly, this is a part of the report supplied by Professor Mitra to, I believe it was to Exela, specifically, Dr. Koneru. But it was to Exela, I believe.

Q. I actually think, it is a little typo -- no. That is correct. I am sorry. And, Dr. Stella, if you need to look at, in your binder, we should have PTX-14. It's the last

document in your binder. If you want to look at it just to make sure.

A. **This is the document that I was referring to. Exela Privileged and Confidential Information.**

Q. **This is the brimonidine corneal permeability and IOP reduction study given to the FDA?**

A. **I believe so, yes.**

Q. **And the pH in this document that we have excerpted is 6.9?**

A. **That's correct.**

Q. **And the pH was not given to the FDA. Is that right?**

A. **To the best of my knowledge, that is the case.**

Q. **All right. Now, did you rely on any testimony from Dr. Koneru about that rabbit testing?**

A. **I believe, in his deposition, he was asked whether the formulation that was used in the, the formulation that was used in the Mitra study was the same formulation that was the ANDA formulation.**

Q. **We will put that excerpt on the screen. What did he say that it was?**

A. **He said that the rabbit testing was done on the formulation that was the subject of the ANDA.**

The answer was: I believe so.

Q. **Dr. Stella, based on all that information, the stability data, long-term and accelerated from the ANDA, the**

stability data from the Exela India, and the rabbit study, did you reach a conclusion as to whether the Exela product would infringe the third element of the claim, the composition having a pH of about 7.0 or greater?

A. **It's my belief that they cannot produce a product that will be in the range of 6.5 to 6.7 without infringing the pH element of the first claim of the '834 patent.**

Q. **All right. I think, then, we can check off that last box.**

Does that mean the Exela product will infringe Claim 1 if, as represented to the FDA, it has the 6.5 to 6.7 release specification?

A. **Yes.**

Q. **Let's take a look at some of the other claims. We can go through this fairly quickly, because they are very similar.**

I am going to put up independent Claim 10. If independent Claim 1 is infringed, is independent Claim 2 infringed for the same reasons?

A. **Yes, it is. The only difference is in the second element. In the second element, in addition to the brimonidine tartrate, it calls for other salts or esters thereof. And, therefore, since the brimonidine tartrate would be included in that element, it includes brimonidine tartrate.**

Q. **Is it your opinion that the Exela ANDA, if the release specification applies, will meet all the elements of Claim 10?**

A. **Yes.**

Q. **Now we will go to the next demonstrative slide, which includes Claims 2, 3, 4, 11, 12, and 13.**

Looking at Claim 2, 3, and 4, is it your opinion that the Exela product will meet those additional limitations in the dependent claims?

A. **Yes. The only difference is that Claim 1 is up to about .15. Claim 2 is up to .15. The third claim is about .15. And the final one includes .15. And the Exela product is said to contain .15.**

Therefore, it meets all three of those claims.

Q. **I think we skipped over a slide. That was the slide we skipped (indicating).**

That is the same slide we looked at before?

A. **That's correct.**

Q. **Then we have the same elements depend off of Claim 10 as well?**

A. **Claim 10, which are the same. I don't think it is worthwhile repeating it.**

Q. **The Federal Circuit makes me do this, so I am just going to ask. Is it your opinion that the .15 percent brimonidine that we just looked at meets the additional**

elements in Claims 11, 12, and 13 on the Slide ADX-31?

A. **Yes.**

Q. **Let's look at a couple other things from the Exela proposed brimonidine product.**

What are we looking at here, Dr. Stella?

A. **This is a side-by-side comparison of the formulations. And you will notice that in the Alphagan P product, it contains sodium carboxymethylcellulose. The Exela brimonidine tartrate formulation .15 does not include an anionic cellulosic polymer.**

Q. **That is from PTX-288 at EX-000037?**

A. **Yes.**

Q. **That is the Exela ANDA?**

A. **That's correct.**

Q. **And let's take a look at the dependent claims 8, 9, 17 and 18.**

What are the additional claim elements in Claims 8 and 9?

A. **Claims 8 and 9, which refer back to Claim 1, requires that the product be substantially free of anionic cellulosic derivatives. Specifically, in Claim 9, is free of carboxymethylcellulose. And they relate back to Claim 1 in the Exela product, it is free of both those elements.**

In Claim 17 and 18, they refer back to independent Claim 10. It has the same elements, free of

anionic cellulosic derivatives and free of carboxymethylcellulose.

They would meet those claims.

Q. **Is it your opinion that Excela's brimonidine product infringes Claims 8, 9, 17, and 18 as you understand the proposed product to be?**

A. **Yes.**

Q. **Let's look at one other thing from the ANDA, which is excerpted from PTX-288 at EX-000037.**

What are we looking at here, Dr. Stella?

A. **This is a list of the inactive ingredients. It shows that the Exela product contains benzoalkonium chloride, a quaternary ammonium preservative.**

Q. **I apologize for the photocopy quality. This is the best quality that was produced to us.**

What is benzoalkonium chloride?

A. **It's as a quaternium ammonium preservative.**

Q. **Let's look at the dependent Claims 6, 19, 20, and 21.**

What are the additional elements in Claim 6?

A. **Claim 6 relates back to independent Claim 1. It says, "Which further comprises a preservative selected from a group consisting of an oxychloro and a quaternary ammonium compound in the amount effective to at least assist in preserving the composition."**

Q. **The benzoalkonium chloride is a quaternary ammonium**

compound that is being used or supposed to be used to preserve the composition?

A. **That is my understanding.**

Q. **Let's look at Claim 19. What does that add to Claim 6, which we just looked at?**

A. **It says that the specific quaternary ammonium compound is benzoalkonium chloride.**

Q. **Looking at Claims 20 and 21, what is the difference in Claim 20?**

A. **The composition of Claim 10 which further comprises, I believe it's similar to Claim 6.**

But referring back to Claim 10, consisting of an oxychloro compound and a quaternary -- from a group consisting of oxychloro component and a quaternary ammonium component in amount effective at least assist in preserving, I believe Exela meets that requirement.

Q. **That is because of the benzoalkonium chloride that we looked at?**

A. **That's right.**

Q. **Claim 21 looks to be similar to Claim 19.**

A. **Right. And that specifically states benzoalkonium chloride.**

Q. **Is it your opinion that the Exela proposed product, as you understand it, infringes Claim 6, 19, 20 and 21?**

A. **Yes.**

MR. SINGER: That concludes my examination, Your Honor.

THE COURT: Okay. Mr. Boggs, start your cross.

MR. BOGGS: Yes.

CROSS-EXAMINATION

BY MR. BOGGS:

Q. **Good afternoon Dr. Stella.**

A. **Good afternoon.**

Q. **You have been working on this case for a number of months. Right?**

A. **Yes.**

Q. **Probably pretty close to a year?**

A. **I don't remember when we started.**

Q. **Before that, you worked on the Alcon case involving the same patents. Is that right?**

A. **I believe so, yes.**

Q. **And you had your deposition taken. Is that right?**

A. **That's correct.**

Q. **In fact, I took your deposition. Right?**

A. **Yes.**

Q. **That was on December 12th, 2008. Right?**

A. **I believe that's correct, yes.**

Q. **That was in Lawrence?**

A. **Yes.**

Q. **And Mr. Marsden was there. Right?**

A. **I believe so, yes.**

Q. **You have given a lot of thought to your direct examination that you just gave. Right?**

A. **That's correct.**

Q. **And you know there are some difficult questions involved in this case. Right?**

A. **Yes.**

Q. **And you have given some thought as to how you are going to answer to those difficult questions. Right?**

A. **Yes.**

Q. **And you are fully prepared to do so. Right?**

A. **To the best of my ability.**

Q. **Now, you mentioned doctor Mitra in your direct examination. You know doctor meet. Correct?**

A. **Yes, I know him very well.**

Q. **You were one of his professors. Correct?**

A. **That's correct.**

Q. **That was about 25 years ago. Correct?**

A. **Is it that long?**

Q. **You were on his thesis committee at the University of Kansas?**

A. **I was.**

Q. **And doctor meet is also a graduate of the University of Kansas. Right?**

A. **He is.**

Q. **Now, Dr. Mitra has focused his career on ophthalmics and is well-respected in the field. Correct?**

A. **Yes, he is.**

Q. **Now, you told me at your deposition that you understood your role in this case to be an advisor to the Court. Is that right?**

A. **That's correct.**

Q. **And you told me that you were going to tell both sides of the story. Do you remember that?**

A. **Yes, of course.**

Q. **Now, target pH, release pH, and shelf life pH, those are three categories of pH associated with ophthalmic products. Correct?**

A. **Yeah. I think it's called manufacturing pH, release pH, and shelf life pH. I don't remember the specific terminology.**

Q. **Some people call target pH manufacturing pH. Right?**

A. **Perhaps. I don't know.**

Q. **Some people call the manufacturing pH compound pH. Right?**

A. **Yes, it can, yes.**

Q. **Then there is release pH. That is the middle one. Right?**

A. **Yes.**

Q. **And some people think that's, as you do, I believe,**

that's the point in time when it is released to the public. Correct?

A. **It is released out of the warehouse and gets to the public, yes.**

Q. **Now, there are also people that believe release pH is when it's released from manufacturing and goes into storage, before it's released to the public. Correct?**

A. **That's not my understanding. But there may be that element out there.**

Q. **Some people also call the release pH the product pH. Right?**

A. **If people use that terminology, I would ask them to define what they mean by that.**

Q. **That's right. Because some people call the product pH the target pH, too. Correct?**

A. **They might.**

Q. **The bottom line is, there is a lot of names for these and they all overlap. Correct? A little?**

A. **There is some confusion, yes.**

Q. **So it is very important that we pay very close attention to what people are talking about. Right?**

A. **That's correct.**

Q. **And sometimes people get confused and make mistakes about what's being referred to. Correct?**

A. **Yes, there is confusion.**

Q. **Now, you put a letter up there that was sent to the FDA about 5.5 to 6.7 being changed to 6.5 to 6.7. Do you remember that?**

A. **Yes, I do.**

Q. **In fact, that is the basis of your opinion of infringement. Right?**

A. **Well, Dr. Mitra also agreed with that.**

Q. **Dr. Mitra did?**

A. **Yes. At his deposition.**

Q. **But did Dr. Koneru agree with that?**

A. **I don't know what Dr. Koneru said on it.**

Q. **Did you talk to anybody and ask anybody if a mistake had been made in that letter?**

A. **I can only go on what I have read and what I have been told.**

So, as I said in my opening, my opening comments, I am very confused as to what Exela plans to do. I can only read the documents and interpret them to the best of my ability.

Q. **Fair enough.**

So you didn't talk to anybody and ask if there was a mistake in the letter. Right?

A. **No, I did not talk to anybody. I read the letter directly, what was stated in the letter.**

Q. **Did you ever consider whether that might have been a**

mistake?

A. **Oh, then I think that should have been corrected to the FDA as well.**

Q. **But did you consider it?**

A. **I don't know -- no, I did not consider it.**

Q. **Well, did you ever check to see if that amendment had ever been made, that proposed amendment?**

A. **It was interesting. Right after that sentence, they said there would be an amendment filed within two days. I don't know of any amendment after that. All I know is they received a letter that eventually said that as presented it would not be approved.**

Q. **I think what you are referring to, I am not sure, but what was missing from this presentation here was the letter that responded to the August 9th letter. Do you remember seeing that?**

A. **I did not see that.**

Q. **No one ever gave you that letter?**

A. **No, I did not see that.**

Q. **No one ever gave you the letter from the FDA that said don't bother changing the pH?**

A. **Not to the best of my knowledge.**

Q. **We will look at that in a little bit?**

JTX-078004. This is the '834 patent. This is the one that you have expressed your opinion on. I want to

look at Claim 1.

Claim 1, the composition having a pH of about 7.0 or greater. Do you see that?

A. Yes.

Q. In fact, you talked about it on direct. Right?

A. Yes.

Q. In rendering your opinion, when you were thinking about all of these things, which category of pH did you consider these, the claims of the '834 patent to be directed to? Remember, we talked about target, release, stability. Which category?

A. At this point, any product at any time which approaches or exceeds the about 7.0, at any time, when made, used, or sold. If it reaches that particular element of about 7.0, it would infringe.

Q. Whether it is at the manufacturing level, the release level, or the stability level?

A. The long-term stability, yes.

Q. By the way, you mentioned pH drift. Is there any mention of pH drift in the '834 patent?

A. There is not, no.

Q. Now, you indicated that Exela's product, that it was your opinion that Exela's product would infringe the patent.

It is also your opinion that if the pH of Exela's product never exceeded 7.0, it would not infringe.

Is that correct?

A. **Sorry?**

Q. **If Exela's product never exceeds 7.0 -- excuse me. If Exela's product never exceeds 6.7 as a pH, it would not infringe. Correct?**

A. **If it never exceeds under make, use or sell, that's correct.**

Q. **So as long as Exela's at 6.7 or below, it would not infringe. Correct?**

A. **At any point during manufacture, release, or sold, yes, I agree that at that point it would not infringe the patent.**

Q. **Now, if it were true that that amendment had never been made, the one that you are basing your theory of infringement on, if that had never been made, would the Exela product infringe the '834 patent?**

A. **Could you restate that? I am a little bit confused on it.**

Q. **Fair enough. If the amendment, the one referred to in the letter that you are relying upon, if that amendment had not been made --**

A. **Sorry. The amendment? What amendment?**

Q. **Okay. Do you recall during your direct testimony there was a letter, and the letter referred to a proposed amendment of the pH specification to 6.5 to 6.7? Do you**

remember that?

A. **Yes.**

Q. **That amendment is what you are basing your opinion of infringement upon. Correct?**

A. **Yes. If that pH was the pH of the product and it had to be maintained in that pH, then my infringement opinion is that you cannot maintain the pH in that range without producing a pH higher than the 6.7, which would then infringe on the '834 patent.**

Q. **If that amendment had not been made, or has not been made, would the product, as described in the Exela ANDA, infringe any claim of the '834 patent?**

A. **In other words, if the product -- can I ask for a clarification on that?**

THE COURT: Yes.

THE WITNESS: If the product is manufactured, made, sold, et cetera, never exceeds 6.7?

BY MR. BOGGS:

Q. **Yes.**

A. **If that is the case, I do not believe that it infringes, although I also believe it would never be approved by the FDA without clinical trials. That is not a legal question. That is a regulatory issue.**

Q. **You don't work for the FDA, do you?**

A. **That's right.**

Q. **You work for the University of Kansas?**

A. **Yes.**

Q. **And we are glad to have you.**

Dr. Stella, these four categories here that you spoke about, each one of those that you testified about, you went to the ANDA to get your information. Correct?

A. **That's correct.**

Q. **You relied on information in the ANDA for the top, for the first one, information in the ANDA for the second one, information in the ANDA for the fourth one. Correct?**

A. **That's correct.**

Q. **For the third one, you went to the letter, and the -- the letter we spoke about with the proposed amendment, and some data from India. Correct?**

A. **That's correct. Also the data, the 6.9 from Mitra's bioavailability study and the noted pH of his formulation.**

Q. **That bioavailability study, did you notice in the letter that it referred to that formulation as an exploratory formulation?**

A. **I would hope that they would not supply to the FDA an exploratory formulation which they are then claiming bioequivalency of.**

Q. **I think they were just submitting data from an exploratory formulation. Correct?**

A. **And they are giving it to the FDA as evidence for**

bioequivalency?

Q. **Whether that's a good way to do it or not --**

A. **It's an illegal way to do it, sir.**

Q. **They identified it as an exploratory formulation. Did you notice that in the letter?**

THE COURT: I guess the question is, Doctor, did you notice it?

THE WITNESS: I did not notice it.

BY MR. BOGGS:

Q. **Okay. So, as I understand it, you believe that if Exela changed its ANDA from a shelf life or stability pH of 5.5 to 6.7 --**

A. **Sorry. Say that again?**

Q. **If Exela changed its ANDA to require a shelf life or stability pH from 5.5 to 6.7 to 6.5 to 6.7, that would require Exela to make the formulation in an infringing way. Is that correct?**

A. **I would also state that if it was 5.5 to 6.7 and in producing that as a shelf life product they produced a product that was about 7.0, it would also infringe.**

Q. **Why is that?**

A. **Because if they made it or sold it or distributed it at any point with a pH -- during manufacturing, for example, if the pH was 7 and yet the shelf life of the product was still 6.7, it would infringe, as long as they made. Sold,**

or distributed the product at pH's of about 7.0, it would infringe.

Q. **What if they made it at 6.5, released it at 6.2 to 6.7, and then it had a shelf life or stability pH of 5.5 to 6.7. Would that infringe? In fact, Exhibit EDTX-133, now, this is the proposal that we were talking about. Correct?**

A. **That's correct.**

Q. **And this letter, in this letter, it refers to a change of 5.5 to 6.7 to 6.5 to 6.7. Right?**

A. **That's correct.**

Q. **And as I understand it, you are not aware of any evidence that that proposed amendment has ever been made. Correct?**

A. **No. This is the last letter that I saw that was an exchange between Exela and the FDA.**

Q. **Okay. Now, an amendment to an ANDA requires a special form. Correct?**

A. **I am actually not privy to that. I assume -- I will take your word for it.**

Q. **You have never heard of Form FDA 356H?**

A. **No, I have not.**

Q. **Did anyone ever show you a Form FDA 356H that indicated that the pH had been changed from 5.5 to 6.7 to 6.5 to 6.7?**

A. **No.**

Q. **All you have seen is EDTX-133. Correct?**

A. **Yes, and also, the -- some comments from Professor Mitra in his deposition. Also, some comments from Stokely and also are some comments from Friedly.**

Q. **From those comments, you drew the inference that the change had actually been made?**

A. **Yes, I did, yes.**

Q. **But you never confirmed that. Right?**

A. **No. I saw nothing, as I said, post this document.**

Q. **Now, this is the letter that I was referring to before.**

This is the response that they got from the --

A. **Yes.**

Q. **-- from the FDA.**

A. **Sorry, this is what?**

Q. **This is the response that they got from the FDA?**

A. **From the FDA, all right.**

Q. **"The differences in pH alone have not demonstrated to account for the ability to alter the innovators' formulation to a lower strength and still maintain the efficacy. Consistency in pH, without the same ingredients, cannot be used to assure equivalent efficacy."**

That was the response they received?

Now, knowing that, knowing that there is no formal amendment made, do you think Exela has amended?

A. **I have no idea what you just asked me.**

Q. **How do you interpret Item No. 3 on this letter?**

A. **I think what the FDA is saying, that there is a holistic issue associated with the formulation, that it depends on all the components of the formulation, and it's saying that pH alone may not account for everything. It's the whole formulation.**

And, therefore, they are asking that the work that was done in the ANDA was not enough to assure the FDA that you had an equivalent product.

Q. **This is the first sentence of the letter. "This facsimile is in reference to the bioequivalency data submitted on August 9, 2007."**

That was the letter with the proposed pH change. And this is the response that they received. Correct?

A. **Mr. Boggs, you have got me totally confused now. This is a letter from the FDA to Exela?**

Q. **Yes.**

A. **So this is a response to the letter that they -- okay. This is not the amendment. This is another letter that they got from --**

Q. **Do you remember when the letter proposing the amendment was sent?**

A. **Yes. August 7th, 2000 -- August 3rd, 2007.**

Q. **And this is the response. Correct?**

A. **Okay. That's right. That was the letter to the FDA. That's correct, sorry, I was getting confused there.**

Okay. So this came from the FDA after that document, okay.

Q. **Right. I take it you have never seen this letter?**

A. **No, I have not seen this letter before.**

THE COURT: Would this be a good point to break for lunch? Bore.

MR. BOGGS: Sure.

(Luncheon recess taken.)

THE COURT: Please take your seats.

Doctor, good afternoon.

Mr. Boggs, you may continue.

MR. BOGGS: Thank you, Your Honor.

BY MR. BOGGS:

Q. **Dr. Stella, this document here, I don't have the PowerPoint presentation, it wasn't provided to me, but I will try to trace back through the documents.**

MR. SINGER: For the record, I object. We did give you the PowerPoint presentation prior to your opening.

MR. BOGGS: We don't have the electronic version.

BY MR. BOGGS:

Q. **Do you recognize this document here?**

A. **Yes, I do.**

Q. **What is this?**

A. **I believe this is the data that was from some stability work that was done in India, I believe.**

Q. **Is this the stability work that you used to generate that graph?**

A. **Yes, I believe so. I am not sure if it's this one or the next one. It is one of these.**

Q. **How would we check that?**

A. **I believe the PDX number is at the bottom left-hand corner of the slide.**

Q. **Okay. This is the chart that you produced from the results in India. Is that correct?**

A. **I believe so, yes. Not I believe. It is, yes.**

Q. **And that formulation had exactly the same formulation as the one that Exela is seeking approval for at the FDA?**

A. **I would have to look at the formula.**

Q. **You don't remember?**

A. **No, I don't remember. I think I think there may have been a slight difference. But I don't remember if it is exactly the same.**

Q. **Here is your expert report. Correct? Page 13. Up at the top, here is the location in your expert report, "The pH stability studies from formulation development in India show that, for a formulation with a target pH of 6.85, designated as 5BT0S08." Do you see that?**

A. **Yes.**
Q. **What is the 5BT0S08?**
A. **I see it as a lot number, formulation number.**
Q. **The 6.85, during your deposition in Lawrence, you told me it is difficult one way or another to decide whether 6.8 would infringe. Is that correct?**
A. **That's correct.**
Q. **05BT0S08, this was something that was prepared in India. Is that right?**
A. **That is my understanding.**
Q. **Now, in the far right column -- we will need the left column -- I decided I wanted to check out what the formulation was. I found this. You weren't asked about this on your direct examination. Right? This document?**
A. **No.**
Q. **What is a buffer used for?**
A. **It's used to try to control pH.**
Q. **Control pH. Right?**
A. **Yes.**
Q. **This Indian formulation has a different buffer than the Exela formulation. Correct?**
A. **I would like to see it side-by-side. But if you --**
Q. **You don't remember?**
A. **I don't remember. I don't remember the exact ingredients. I have seen so many formulas over the last**

couple days...

Q. **.15 brimonidine tartrate?**

A. **Right.**

Q. **It looks like it has a complex combination of a borate and citrate buffer. Right?**

A. **I notice that, yes.**

Q. **Do you remember the Exela formulation, as they are seeking approval for, having a borate buffer or any borate component to it?**

A. **You know, I don't think it does. But, again, if you are going to ask me that comparison, I would like to just confirm that.**

Q. **Fair enough. We will look at that in a little bit.**

A. **If you attest that it doesn't contain borate, I am comfortable with that.**

Q. **We will get it up here. Okay. You can see the Exela formulation there in the middle.**

Do you see any borate or boric acid in the Exela formulation?

A. **No, it does not.**

Q. **Okay. So, can we conclude, sitting here right now, or standing here right now, that the formulation from India from which you were drawing your conclusion about pH, and where the pH has to be, has a different buffer than the Exela formulation?**

A. **Yes.**

Q. **And it is the buffer in a formulation that controls pH?**

A. **Yes. It should attempt to control the pH, yes.**

Q. **Do you remember noticing that when you gave your opinion?**

A. **Actually, no, I did not notice that. In fact, I am not sure that I had the formula.**

Can I ask a question?

THE COURT: You have to wait until Mr. Boggs asks.

THE WITNESS: Okay.

BY MR. BOGGS:

Q. **Now, your proposal for meeting the specification that we were talking about before lunch was to raise the pH up high, above 7.**

There are other ways in formulation work to control pH, focus the pH of a particular area. Right?

A. **I don't know what you mean by that.**

Q. **Isn't it true that you could satisfy the pH requirement of 6.5 to 6.7 by using phosphate buffer?**

A. **Yes.**

Q. **So that's an alternative to manufacturing above 7. Right?**

A. **Yes.**

Q. **And another way to control the pH would be to increase the buffer concentration. Right?**

A. **It can help, yes. It should help.**

Q. **Or you could just specify that the product needs to be refrigerated to meet the shelf life. Is that an alternative?**

A. **It's an expensive alternative. But it is an alternative. You are making the assumption that refrigeration slows up any deleterious process that swings the pH, that's correct. I don't have any experience in that, in ophthalmic products with refrigeration, but, hypothetically, it could help.**

Q. **Insulin products, for example, are refrigerated. Right?**

A. **There is a lot of refrigerated products. That is usually due to chemical stability issues.**

Q. **Or you can simply reduce the shelf life from 24 months to 18 months or whatever?**

A. **There are some products that have shorter than two-year shelf lives.**

Q. **So there are other alternatives than manufacturing at a pH higher than 7. Right?**

A. **There could be, yes.**

Q. **Here we are again, Dr. Stella. I want to talk to you about the last item on this list. Soluble in the**

composition at about 21 degrees C. Do you see that?

A. **Yes.**

Q. **I am a little concerned about this. I heard you say that there was no dispute about it. I also heard you say that you noticed from the ANDA literature that the product was in solution and therefore it's soluble?**

Is that your logic?

A. **Yes. That both the Alphagan P and the Exela formulations claim that it is an ophthalmic solution.**

Q. **Okay. Now, there are different gradients of solubility. Would you agree with that?**

A. **Yes. Standard textbooks often give a range. But they are controversial as to what they encompass. But, yes, there is some reasonable numbers out there that people use generally, yes.**

Q. **And the categories are, there are several different categories. Correct?**

A. **Yes. I don't remember them all, in terms of technical names.**

Q. **If you wanted to find out what they were, how would you do that?**

A. **Go to some literature, go to a textbook.**

Q. **Would you go to Remington's?**

A. **It's one book in our field, yes.**

Q. **I think in your textbook, or in your book, you have an**

excerpt from Remington. Do you see that?

A. **Can you tell me what the number is?**

Q. **Well, it has no number. It's just in there, near the back. It says Remington's 1953. It should be a tab.**

A. **56.**

Q. **56, that's right. Do you see that?**

A. **Yes.**

Q. **I see a chart in this document which caught my eye. Do you see that chart? It's about three pages in. Page 149?**

A. **Yes, I see that.**

Q. **Up at the top left, do you see that?**

A. **Yes.**

Q. **It says, Very Soluble, Freely Soluble, Soluble. There is a category, Soluble, Sparingly Soluble, Slightly Soluble, Very Slightly Soluble, Practically Insoluble, or Insoluble.**

At least five of those seven are in solution?

A. **Correct.**

Q. **There are seven categories there. Right?**

A. **Yes.**

Q. **Of those seven, there are at least six solutions?**

A. **This is not saying that they are in solution. This just says that if you take a drug, for example, that is considered to be very soluble and you mix one part of drug with one part of solvent, you will have a drug in -- below**

that ratio, you would have the drug in solution.

In excess of that, if you have more than one -- less than one, right. So, in that case, the one that is always in solution when you take that drug would be the first one, for the most part. Even in the second one, it says that, actually, if you have one part of drug and less than one part of solvent, it would be a suspension. This is just defining the range of conditions under which you would put a solute to have the drug in solution and outside of, at the upper end of that range, it would be in a suspension.

Q. **When you were rendering your opinion in category 4, did you do any measurements like that?**

A. **Why would I do any measurements, sir?**

Q. **Well, I see soluble. And there is numbers next to it. It seems to me that you would need to do a measurement?**

A. **There were measurements -- there were solubility measurements in the patent, and when the -- in the ANDA, and when we did the comparison, both sides had agreed -- not agreed, the ANDA says that they have a solution. It is a solution of .15 percent brimonidine tartrate. I don't understand where you are going?**

Q. **It is a solution, therefore, it's soluble. That is the logic you applied. Right?**

A. **The word "solution" means that it's not a suspension.**

Q. **Right. It could have some particulates in it. Right?**

A. **Sorry?**

Q. **Soluble, something that is soluble, if it's in solution, it can have some particulates in it?**

A. **Well, it would have -- not the drug particulates, but it would have a particularity -- there is a particularity requirement in ophthalmic products. You cannot have particulates and call it a solution if it's an ophthalmic solution.**

It then would render the product outside the specifications, I believe.

Q. **Very soluble, soluble, freely soluble, different categories.**

I was looking at this chart. 6.7, the solubility is very high. Correct? On this chart?

A. **It has some limiting solubility at 6.7, but it's off that chart, that's correct.**

Q. **It is off the chart.**

7.2, 7.3, it is much lower?

A. **Yes.**

Q. **And we do know from the patent that that level is soluble.**

A. **Below, at concentrations below those lines, it's soluble.**

Q. **So a formulation that has a pH of 6.7 is going to be much more soluble than one at 7.2 or 3?**

A. **For brimonidine tartrate, that's correct.**

Q. **So it is very soluble, isn't it?**

A. **Sorry?**

Q. **It's very, very soluble at 6.7?**

A. **Again, I would have to look at the definitions, do the calculation numbers and tell you which category it fits into.**

Q. **I agree.**

Now, I was concerned, I had this 1956 -- have you seen this chart, by the way, before?

A. **I have seen charts like this. If you pick up -- I don't know if that is a rigid classification. It might be. But I have seen charts. I don't use it.**

Q. **Well, I was concerned that it was out of date or out of style?**

A. **People usually just report the solubility.**

Q. **You have this in your book, too. This is another Remington. Dr. Olejnik said he prefers Martindale. Do you like Martindale?**

A. **It depends if you come from the British system or the American system.**

Q. **This is much newer in the 2000s. If you turn four pages, Table 16.1 at the bottom, we see it again. "Very soluble, freely soluble, soluble, sparingly soluble, slightly soluble."**

So will you agree with me that it is not out of date?

A. I never said it was outdated. Just that a lot of people use this and other people don't. This is not a hard-and-fast rule that people use.

Q. And then the next one, I just wanted to check the 1990. I didn't have a Remington sitting around my room. I had Physical Pharmacy from the 1990s. Table 10.1. There we see it again.

Will you agree with me that this seems to be an acceptable way of characterizing solubility?

A. Yes. I mean, I am not disagreeing with that. In the case of a drug like -- can I explain?

Q. He will have a chance.

A. Okay.

Q. In fact, I am going to give them a chance right now. I don't have any further questions.

THE COURT: Thank you. Mr. Singer.

REDIRECT EXAMINATION

BY MR. SINGER:

Q. Very briefly, apropos, since I am here, why don't you explain what you wanted to say with regard to counsel's question about solubility.

A. It is just that that classification doesn't take into account for an ionizible drug, the solubility will vary as

pH various. That is all I needed to say.

Q. **Brimonidine is an ionizible drug?**

A. **It is an ionizible drug, so if you put brimonidine tartrate into water, you would have a particular solubility, and, therefore, it would fit into that classification at one pH value and it would slide through that classification as you change pH.**

Q. **I would like to put up EDTX-171.**

This was the letter from the FDA, just to remind everybody, in response to the letter that you relied on, Dr. Stella.

Do you recall seeing this with counsel?

A. **Yes, I did.**

Q. **I would just like to go over a couple things that weren't highlighted by counsel. I first would like to go to the second paragraph right there, and I will read this. It says -- this is in response, correct, to the August 9, 2007, letter?**

A. **I assume it is, yes.**

Q. **It says, "The division of bioequivalence has completed its review of the submissions referenced above and has identified deficiencies which are presented on the attached page."**

Did I read that correctly?

A. **Yes.**

Q. **And "this facsimile is to be regarded as an official FDA communication, and, unless requested, a hard copy will not be mailed."**

Did I read that correctly?

A. **Yes.**

Q. **Is that what the FDA said in response to the Exela letter of August 9, 2007, in part?**

A. **That appears to be the case, yes.**

Q. **And then I would like to go to the next paragraph and highlight the first sentence. It says, "You should submit a response to these deficiencies in accord with 21 C.F.R. 314.96. Your amendment should respond to all the deficiencies listed."**

Do you see that?

A. **Yes.**

Q. **Dr. Stella, have you seen any response to this bioequivalency amendment from the FDA?**

A. **Not to my knowledge.**

Q. **Go to the next page. There are some other things that weren't pointed out. If we could highlight the paragraph that says, "In the current correspondence." I will read this. It says, "In the current correspondence, you have not submitted any new information or data to address adequately the deficiencies communicated to you in our previous letter. You have not provided any new evidence necessary to**

demonstrate that the differences between the test and RLD formulations do not significantly affect the safety or efficacy of the drug product."

Did I read that correctly?

A. **Yes.**

Q. **For the record, the test formulation, is that the proposed generic formulation?**

A. **Yes.**

Q. **And, then, what does "RLD" stand for?**

A. **Reference listed drug, I believe. This would be the Alphagan P .15 percent.**

Q. **Then the FDA officer goes on to say, "The medical officer of the Division of Antiinfective and Ophthalmalgic Products, Office of Antimicrobial Products, at the agency also has the following comments concerning your original and current submissions."**

Paragraph 1. "The proposed drug product is not the same with respect to the inactive ingredients. The proposed differences have the capability of affecting the efficacy of the drug product."

Did I read that correctly?

A. **Yes.**

Q. **I have one more thing, then I have a question for you. At the bottom, it says, "For the reasons listed above, our previous recommendation for denial of your waiver request**

has not changed."

Do you see that?

A. **Yes.**

Q. **I believe we talked a little bit on direct examination about what a waiver request was. I think you testified that it's a request to waive the requirement to do clinical trials. Is that your understanding?**

A. **I believe that's my understanding.**

Q. **Have you seen, in your infringement analysis, any clinical trials performed by Exela in response to this FDA request?**

A. **No.**

MR. SINGER: I have nothing further, Your Honor.

THE COURT: Doctor, thank you.

THE WITNESS: Thank you.

(Witness excused.)

MR. MARSDEN: Your Honor, that completes our affirmative case. We just wanted to understand how Your Honor wants to handle exhibits. We referred to them, obviously, throughout the trial. This is a Bench trial. I didn't know whether you're going to want us, at some point, to submit a list of those we referred to during the testimony.

THE COURT: A list might be helpful, Mr. Marsden. We have, of course, received Bench books. I

should think that a general list, a list more particularized, or that you want me to pay close attention to, both parties.

MR. MARSDEN: We can provide that, Your Honor.

MR. BREISBLATT: Your Honor, may I ask a question?

THE COURT: Sure.

MR. BREISBLATT: Earlier in the proceeding, I think somebody, and I forget who it was, went to move an exhibit in. The Court noted that, since we had done lists, they were all admitted.

Now, that's what I now need clarification on.

May we use -- so, for example, if we do findings of fact and conclusions of law after the case, can we refer to exhibits that are on the exhibit list even though no witness referred to them?

THE COURT: Yes.

MR. BREISBLATT: So what the Court said is all the exhibits on that list are in, and we don't have to stand up here and move them in.

THE COURT: That's correct. Absent an objection, my blanket procedure has been to admit. Thus far, no exhibits on the list have been contested, beyond that ruling.

MR. BREISBLATT: The reason I ask, I know we

made some objections to some of their exhibits. They made objections to some of those, 403, that kind of thing.

THE COURT: There was a listing of objections. But those have been summarily dealt with. Unless there is an issue with any future exhibit --

MR. BREISBLATT: The reason I ask, it will shorten some of our examinations. In some courtrooms, a judge won't allow an exhibit to be used unless someone touched it or saw it.

THE COURT: We all do it differently. That is a process I adopted from your hometown, a Northern District judge out of Chicago. I find it, I have found it, over the course of the years, to be an effective process.

MR. BREISBLATT: That makes it fine, Judge. That will simplify our case.

MR. MARSDEN: One other housekeeping matter, Your Honor. You may recall that we moved in limine to preclude some of the expert testimony. Your Honor denied that but allowed us to do supplemental expert reports. In doing so, there were some exhibits identified in those supplemental reports. We provided an updated trial exhibit list to the defendants. We have not yet provided that to the Court. I can do that now and we can also file it so it's of record.

THE COURT: Let's see if there is a problem with

that.

MR. BREISBLATT: No, Your Honor.

THE COURT: That is fine, Mr. Marsden.

Are we ready?

MR. BOGGS: May I be heard, Your Honor?

THE COURT: Yes, sir.

MR. BOGGS: Your Honor, Exela moves, under Rule 52C, for judgment as a matter of law on the matter of infringement. We don't believe they have offered evidence on the issue of soluble in the claim, and, also, the Exela formulation, as described in the ANDA, does not meet the about 7.0 or greater limitation of the claims.

THE COURT: Okay. I will reserve on that.

MR. BOGGS: Thank you, sir.

MS. BROOKS: With that, Your Honor, Allergan rests its case-in-chief.

THE COURT: Thank you, Ms. Brooks.

Who is going to start?

MR. BREISBLATT: Your Honor, I think the way the Court has suggested this be done is that Exela does its noninfringement case, because you just heard the infringement case and it will make it easier for the Court to follow, then we will do our invalidity case. Then I believe Allergan will have a chance to put on a rebuttal case to the invalidity case.

Did I fairly say that?

THE COURT: I think that comports with our previous discussion, does it not?

MR. SINGER: I think that's right, if I understand it correctly. Just to make sure, Exela is going to present its expert only once, he is going to testify about noninfringement and then validity so we don't have to do this twice.

MR. BOGGS: I only have three witnesses, Your Honor. I would just like to do it all at once, if that is okay.

MR. SINGER: That is fine with us.

THE COURT: You have an agreement.

MR. BOGGS: Your Honor, we have a paper on the 52C.

THE COURT: You want to Bench-file it.

MR. BOGGS: Yes.

THE COURT: I am assuming the other side has it?

MR. BOGGS: They will.

THE COURT: Mr. Boggs, why don't you electronically file that?

MS. FARNAN: I will take care of that.

MR. BOGGS: That is what she recommended as well.

THE COURT: She is right. Given who she is,

absolutely.

MR. BOGGS: Your Honor, our first witness is Dr. Phanesh Koneru. He is the founder, the president, and the CEO of Exela Pharmsci. Dr. Koneru will testify about his unique background and his company, Exela. He will also testify about the product work that was done to development the 0.15 percent formulation for which approval is sought. And Dr. Koneru will testify about Exela's ANDA.

THE COURT: All right, Doctor.

...PHANESH KONERU, having been previously duly sworn as a witness, was examined and testified as follows:

DIRECT EXAMINATION

BY MR. BOGGS:

Q. Dr. Koneru, will you please introduce yourself to the Court by way of describing your educational and professional background and your relationship with Exela?

A. Thank you.

Thank you, Your Honor.

THE COURT: You are welcome.

THE WITNESS: My name is Phanesh Koneru. I am president and CEO of Exela Pharmacia, Inc.

My background includes the legal, business and pharmaceutical fields. I have a Bachelor's degree, I have a Master's degree in pharmaceutical sciences from Andhra, India. I obtained my Ph.D. in biomedical chemistry from the

University of California in Los Angeles. I specialized in biomedical chemistry.

After that, I went to the U.C. San Diego School of Law and I got my J.D. degree from there. Then I graduated from Columbia University School of Law from the LLN program.

THE COURT: What did you do your LLN in?

THE WITNESS: In business law.

After that, I worked in a law firm in New York and another law firm in Palo Alto, California. After that, I went to Watson Pharmaceuticals as an in-house patent counsel.

I was there for about four-and-a-half years. After joining Watson and working there for eight-and-a-half, I became their vice president of intellectual property.

I was a registered pharmacist in California for 12 years. I was a pharmacy manager for most of it.

I am a registered patent attorney, registered at the U.S. Patent Office. I am a member of the California Bar.

Q. **Dr. Koneru, how did you get involved in the pharmaceutical sciences?**

A. **It's a long story. It has its basis from my childhood days in India. It's emotional, so --**

THE COURT: Take your time.

THE WITNESS: I grew up in a rather poor family in India. My family had no fixed assets. My parents could not afford to raise three children, so they sent me to live with my grandparents in a small village. The village had no electricity, no water, or no telephones. I used to walk for a mile to school.

The school had thatched roofs and mud floors, so when it rained, the school would close for a few days.

One day, I was walking to school with my classmate, Ramah, he was about 15, 20 feet behind me, and all of a sudden, I heard a loud scream, and I turned back and I saw him fall to the ground.

I saw a snake, brown snake, passing by. I immediately knew that he was attacked by a King Cobra. There was no antidote available at the time.

And he died within a very short time. And the tragedy affected me.

I decided to become a scientist, a medicinal scientist, to help make medicines.

Q. **In what way did you pursue becoming a medicinal scientist?**

A. **I graduated at the top of the class from my high school, and I was given a national merit scholarship. And I went to Andhra University School of Pharmacy which was about 200 miles away from my place. It's on the East Coast of**

India. The university was the second oldest pharmacy school in INdia. It was built by the British, and the fact is that we were trained under the U.K. I graduated again from the school with honors.

Then I wanted to come to the United States for my higher education.

BY MR. BOGGS:

Q. **How did you find your way to the United States?**

A. **It was not easy. I got admission to the Philadelphia College of Pharmacy and Science here, which is the oldest pharmacy school in the U.S.**

I was given a fellowship. But I couldn't get the visa. I tried about three times, and I still couldn't get the visa from India. The diplomatic relations between India and the U.S. at the time were very poor. All the relations were frozen. I had to take a detour, so I went to Germany, because at the time, Germany did not require any visas. When I went there, I had about $500 in my pocket.

After going there, I realized it was going to cost a lot more money to learn German. I decided to teach myself German, and I did.

I learned German very fast. In about five months, I was fluent to attend the universities in Germany. I was writing and reading and speaking German more fluently. And I got admitted into six universities there.

But before I could attend any of them, I got a visa to the United States. So I came here.

Q. **Where did you go when you went to the United States?**

A. **I went to the University of Southern California School of Pharmacy.**

Q. **What did you do after that?**

A. **I specialized in biomedicinal chemistry. I did my Ph.D. there. While I was doing my Ph.D., I passed the California pharmacy boards. And I became a registered pharmacist. And I started working evenings and weekends as a pharmacist.**

Q. **What prompted you to go to law school?**

A. **As I was working in the pharmacy, I noticed that there were some products that had no generic equivalents. And there were some other products that had generic equivalents coming at the time.**

So I was talking to the presidents of the companies and I asked why some products had generics and the others didn't. And they told me it is because of the patent protection some parties have. And that kind of intrigued me and I wanted to learn more.

I started reading about that. Then it occurred to me that patents are very important for the pharmaceutical industry. And I wanted to be a patent lawyer.

That's one way I could get to the pharmaceutical

industry.

Q. **What did you do after San Diego Law School?**

A. **As I first graduating from San Diego Law School, I realized that one day I would join industry in a senior management position.**

So I wanted to be prepared. And I wanted to learn more about the business side of it. At the time, Columbia University School of Law has some of the best business faculty. So I joined the LLN program, I joined in.

Q. **How did you end up at Watson Pharmaceuticals?**

A. **Watson was one of the clients of the law firm I was working in Palo Alto. And I was advising them on the branded and generic patent statutes. One day, they called me and asked me if I was interested in joining Watson as an in-house patent counsel, and I did. I took the opportunity because I felt that gave me the best position where I could bring to bear all my diverse educate and experiences and bring it to the patent area. And that's what I did.**

Q. **You mentioned you are president and CEO of Exela. What is Exela all about? What's its mission?**

A. **Exela is a pharmaceutical formulation development company. Our mission is to facilitate the entry of generic products to the market at a much earlier rate than otherwise possible. I feel very passionate about this.**

When I was at the pharmacy, I had seen a lot of

people come with prescriptions. But they couldn't get the prescriptions filled. These are elderly people, uninsured, unemployed, otherwise can't afford them.

The people asked me how much it cost, and I would tell them. And I would see the despair in their faces. They practically had to make a decision whether to pay for the medication or rent, or for groceries. I used to feel bad about it. But there is nothing I could do.

When we started Exela, we wanted to make Exela's mission this, which is to make the generic pharmaceuticals and make them, get them into the market at a faster rate.

Q. How would you get them there at a faster rate?

A. Our objective is really to design around patents. To make noninfringing formulations.

Ideally, we would not want to be sued. If the noninfringement is good, then we want to get the 30-month stay on the approval. Because of that we could get to the market faster. That was the business model.

Q. Faster than what?

A. Faster than if you had a 30-month stay, and then you go through the lawsuit, then you have to wait for 30 months again.

Q. Now, what did you do specifically to advance that goal?

A. I teemed up with a classmate of mine, Dr. Mitri. We

were classmates in India when I was doing my Bachelor's and Master's. He was one of the best formulators I know.

We started a lab in India. Our objective is to do the formulation work there. And I would tell him, you know, what the formulation should contain. And then he would formulate it.

Once we formulate, you know, this is an integrative process, where you make several different formulations and you refine it and refine it until you get it right.

Once you feel that you are getting there, then you can start talking to the partnership, talking to different companies for partnerships. That's what I was doing.

So we formulate, we come up with a noninfringement formulation and see that the product is stable. Then we go to a pharmaceutical company here and offer them for licensing.

They will take it up to the next step, which is manufacturing of the product and then filing of the FDA, getting the approval, and then launching onto the market.

Q. Just so we are clear, what is your contribution to the process?

A. My contribution is to help the company come up with a with the noninfringing positions. And I have done this

before several times at Watson.

We have designed around several patents and several products to come up with noninfringing products. We have done this with products that belong to big companies, like Pfizer, Bristol Myers, and also smaller companies, such as Solvey. In some cases, we were not sued. And in a couple cases, we were sued, but once they understood the formulation, the lawsuits were dismissed.

We were able to do that even at Exela. For example, our first product, which we licensed, was a noninfringing formulation. And this was so clear for us that the company did not even bring the lawsuit. Because of that, we were able to get it approved much faster and we were able to launch.

The product was licensed to Teva Pharmaceuticals, which is the largest generic company in the world.

Q. **Dr. Koneru, what is brimonidine?**

A. **Brimonidine is an alpha-2-adrenergic agonist. It is used to treat glaucoma, or intraocular pressure.**

Q. **What brimonidine products are you familiar with?**

A. **I have seen four different approvals for brimonidine at different strengths. They are all in the Orange Book listing, you will see them. The highest strength is .5 percent. Then you have a .2 percent. And you have .15**

percent. And the .1 percent.

The .5 percent or the .2 percent are called Alphagan products. And then the .15 and the .1 percent are called Alphagan P products.

Q. **And did Exela have a brimonidine project?**

A. **Yes, we do.**

Q. **And describe that for us, please.**

A. **It is a generic formulation for brimonidine, for Alphagan P .15 percent.**

Our formulation will contain brimonidine tartrate .15 percent, and then some excipients, which are not in the Alphagan P formulation.

Q. **So, what did you do once you decided to explore brimonidine as a potential candidate?**

A. **I asked Dr. Mitra to start working on the formulation with this drug. I gave him what he should read and he started working on the formulation. We were going back and forth and making several different formulations and see which one would work, which one would be stable.**

As we were doing that, you know, we were also looking at other things.

At one point, he asked me to do the formulation. I did. It looked to be stable. Then, for me, the next thing is, okay, we can make the formulation, it may be stable, and it is noninfringing. But then, will it be

equivalent? Will it be safe and effective? Because we can get a product that is noninfringing, but it is not stable or safe. And if it's not safe or effective, you know, we will not get the approval.

So we looked at the, I started reading up on the FDA approval documents and all the literature that I could find on the clinical studies, on the pharmacology of brimonidine.

After reviewing all of that, it was clear to me that we could formulate the product that is noninfringing and also would be clinically effective and safe.

Q. **Okay. Let's look specifically to the .15 percent Alphagan P.**

A. **Yes.**

Q. **What did you find out from your initial review of the documents?**

A. **The initial review, you know, I looked at the FDA documents, such as the summary basis of approval. And then I also looked at the product labeling of the .5 percent and the .2 percent.**

They are available on the FDA websites. From there, I compared that with the patents, and the patents that I was going for. And I looked at the file history of the patents. Then I also looked at the different articles, publications made by Allergan and others. From that, I

could come up with a noninfringing position, for which I felt good about.

The formulation ideally should have no Purite and no solubility enhancing component. And then it will have a different pH.

And then, also, I felt good that we could come up with a different buffer.

Q. **Okay. Do you recall what the formulations of the original Alphagan were?**

A. **Yes, I do.**

Q. **What were they?**

A. **The original Alphagan had brimonidine tartrate with a .5 percent or the .2 percent. And it had the polyvinyl alcohol as a thickening agent. Then it had the citrate buffer as a buffer component. Then it had the benzoalkonium chloride as the preservative. Then --**

Q. **Did it have a thickening agent?**

A. **Yes. It's polyvinyl alcohol, PVA.**

Q. **And what was the pH of that product?**

A. **The pH of the product, according to the package insert, was from 5.6 to 6.6.**

Q. **Are you familiar with the formulation of the Alphagan P product?**

A. **Yes.**

Q. **What does that include?**

A. **The Alphagan P had brimonidine tartrate .15 percent, and then it had a thickening agent, which is sodium carboxymethylcellulose, then it had the borate buffer. And there you have Purite as a preservative.**

Q. **Did the carboxymethylcellulose have a special function?**

A. **Yes. It was described in the patents as having a solubility enhancing property.**

Q. **And what was the pH of Alphagan P?**

A. **Alphagan P, the package insert said from 6.6 to 7.4.**

Q. **Now, throughout this process, where you were looking at brimonidine, did you look at the Orange Book?**

A. **Yes, I did. That was one of the first things I did.**

Q. **What is the Orange Book?**

A. **The Orange Book is an FDA publication that is not only available online, it shows the drug products that are approved where the therapeutic equivalents as well as the therapeutic equivalents code. And you click the hyperlinks and you will see the patents listed against each product, if there are, anyway.**

Q. **And were there any patents listed for Alphagan P .15 percent?**

A. **Yes. There were five patents listed against the Alphagan P product.**

Q. **Okay. How would you describe those five patents?**

A. **The oldest patent, I believe it was expiring in 2012, covered the usage of the Purite as a preservative. I called it as a Purite patent.**

Then there are four patents that all came from the same family. I think the one was sometime in July 2000. All four patents had the same specification. I call those as the CMC patents.

Q. **What is your understanding of what the CMC patents are about?**

A. **The invention, as I understood it, to be stated, as the product, you know, as you raise the pH of the product, you get more absorption into the system because more drug will be ionized. And when you raise the pH, then you have a problem, which is the solubility. As the pH goes up, then the solubility of brimonidine goes down.**

To solve the problem, the patent states that you need to use a solubility enhancing component to make the brimonidine solution.

Q. **Did you have any preliminary thoughts at the time that you looked at the patents as to whether you could design a noninfringing alternative?**

A. **Yes. I felt confident that I could design around these patents. I could do that by not using the Purite and not using the solubility enhancing component and also keeping the pH lower than about 7.0 or greater.**

Q. **What did you do to investigate that?**

A. **I asked Dr. Mitra to start making formulations to see how they are going to work. Then, also, I have talked to several different consultants to see whether this formulation would be acceptable for filing with the FDA. And we were, obviously, going on.**

As we investigated more into the formulation work, we wanted to really understand the effect of the pH on the Purite. We felt, it has been my thought always that you may be able to get the product filed, but, you know, can we get the approval? And what kind of studies are needed and are we going to be bioequivalent?

I was studying on the effect of the pH on the Purite. So we asked, and I asked Dr. Mitra to work on some kind of invitro study test. And that's what he did. And he found out that the pH has no effect on absorption from the invitro study.

Then we also had some thoughts about the invivo studies. And we decided, we went back to Dr. Mitra's lab, did a rabbit study to see how the formulation at the time would work in the rabbits. And the formulation at the time was evolving. And it was starting to get interesting, but we wanted to see. Because we had already lowered the pH from 7.2 of the product to 6.9. Then we wanted to see how that works. And that's why we had Dr. Mitra's lab -- the

results that I related. And we have the results that showed that the product was bioequivalent. Then we were going to do further studies to lower the pH and then further do the rabbit study.

Q. **Let's back up a step here. It seems to me that if you lower the concentration of brimonidine from the .2 percent level to the .15 percent level, that you are necessarily going to impact the efficacy of the drug.**

What did you find out about that?

A. **Yes. I mean, there is always the concern, I think we heard yesterday in the testimony, that doctors always want to use the lowest effective dose. Again, there will be tradeoffs when you go down. So there is a concern.**

So I read reviewed the literature. And I found one article, which was the Walters article that we talked about yesterday. And it gave me a lot of comfort. I think it was published in 1996. In the Walters article, especially, I remember the Figure 3, where they talked about the rather shorter period, the results of the expert.

There, you will see the study contained the .5 percent and .2 percent and then .08 percent. There was also a placebo there. And the conclusion was that all three strengths were, effectively lowered the intraocular pressure with at all ten points.

I understand that they were practically

comparable in their efficacy.

THE COURT: What was the three strengths?

THE WITNESS: .2 percent, .5 percent, and .08 percent, three strengths. That assured me that by lowering the concentration, you could still have an effective product. And as you are lowering, you could go all the way up to 0.08 percent and still have an effective product. So I did not have any concerns that the product would not be effective.

BY MR. BOGGS:

Q. **We were talking about the Alphagan, the original Alphagan product a little while ago. Why didn't you just pursue the original fact product?**

A. **You mean the original Alphagan?**

Q. **The .2 percent.**

A. **The .2 percent. The product was discontinued by Allergan, because they have introduced the .15 percent. And, in fact, I saw a citizens' petition that was answered by the FDA, in which the FDA said that the product was not withdrawn from the market for safety or efficacy reasons. It was purely for commercial reasons that they withdrew it. So that told me, by looking at that, it told me there was no safety or efficacy issue with the previous product. And now the vehicle that they had had no safety or efficacy issues. So I could use that vehicle and I also would not have any**

safety or efficacy issues with that.

Q. **By "vehicle," what are you referring to?**

A. **I am referring to all the other excipients except the active ingredient.**

Q. **And that would include the preservative?**

A. **Yes. That would include the preservative, the thickening agent, and the buffer.**

Q. **Did you ever figure out why Allergan discontinued the Alphagan product?**

A. **Yes, I did. I am familiar with the strategy. It's called lifecycle management. Basically, what some brand companies do, they try to --**

MR. SINGER: I am sorry to interrupt. I want to interpose an objection. It seems to be in the zone of expert testimony of what branded companies do as a general matter.

THE COURT: I don't know that it is expert testimony. He worked in a branded company.

MR. SINGER: I don't think he worked in a branded company.

THE WITNESS: I did.

THE COURT: I am going to overrule the objection.

MR. SINGER: Thank you, Your Honor.

THE WITNESS: The strategy is to, as you are

getting closer to the time period where you don't have product exclusivity or you are expecting generic competition, you make the next generation product, making some formulation changes or some other changes. Sometimes trivial; sometimes meaningful, then you will get patent protection for it. Then you withdraw the product that was there before from the market. Then you force the substitution of the treatment into the new product.

With that, you have an extended monopoly for a long time. And, for the generics, the product is withdrawn from the market so there is really nothing there to compete against, because even if you make a generic for the withdrawn product, that cannot be substituted for the new product.

Q. **Back to the reformulation, once you were satisfied that you could reformulate Alphagan .15 percent, what did you do?**

A. **I started talking to partners. One of the partners was Paddock, there was a doctor, they were interested in this. So we got together and we had an agreement signed up quickly after that.**

They hired Pharmaforce to do contract manufacturing, and that's where the ANDA batch was made.

And then we had filed the ANDA.

Q. **I thought I heard you mention Paddock.**

A. **Yes.**

Q. **You are going to have to speak up a little bit.**

What role did Paddock play?

A. **Paddock was involved with contract, because Paddock, itself, I don't believe, had any manufacturing capability for these kind of products. So they went to Pharmaforce and had the product made. And the ANDA was filed, while they still had the rights on the ANDA, and the ANDA was filed. And after that, I got the acceptance letter from the FDA. Once I received the acceptance letter, I sent the notification letter to Allergan, as per the statute.**

Q. **Whatever happened to Paddock?**

A. **After we got sued, they had some private conversations with Allergan. I was not privy to them. Then they came up with an agreement. That's the last I heard of them.**

Q. **Okay. Dr. Koneru, Exela has filed an ANDA directed to the .15 percent formulation. Correct?**

A. **Yes.**

Q. **I would like you to look in your book, if you would, I would like to direct your attention to JTX-124. Excuse me, EDTX-124.**

A. **Yes.**

Q. **I would like you to take a look at that document and tell me if you recognize it.**

A. **Yes, I do.**

Q. **What is it?**

A. **It is the publicly available copy of the Alphagan .5 percent approval document from the FDA.**

MR. BOGGS: May I have a moment, Your Honor?

THE COURT: Yes, sir.

(Pause.)

MR. BOGGS: I am sorry, Your Honor. A little confusion.

THE COURT: Counsel, while you are taking a few minutes, let's take a stretch.

MR. BOGGS: Thank you, Your Honor. I appreciate that.

(Recess taken.)

THE COURT: Counsel, let's be seated, come to order, and, Mr. Boggs, are you ready?

MR. BOGGS: Thank you, Your Honor. We discovered the error.

It is EDTX-129. The problem that we had was the back was in the front and the front was in the back. It should be the cover letter for the ANDA. The reason we presented it this way is we have nine boxes back here --

THE COURT: You don't have to explain.

What is the exhibit?

MR. BOGGS: EDTX-129.

Then the white notebook that you have in your

hand are little excerpts from the handbook, there were nine boxes.

THE COURT: 129 is in Volume 1 here.

MR. BOGGS: Yes, 129. Then if you open it up, Volume 3, if you open up 129, you should see what I saw, which is an appendix or something.

THE COURT: I see an executive summary. But it says, "Appendix D."

MR. BOGGS: Yes. The Appendix D goes in the back.

THE COURT: I am with you. I see the letter.

MR. BOGGS: Thank you.

Sorry for that.

BY MR. BOGGS:

Q. **Dr. Koneru, do you have 129 in front of you?**

A. **Yes, I do.**

Q. **And do you recognize that document?**

A. **Yes, I do.**

Q. **What is it?**

A. **It's a cover letter from the ANDA file that we made for the FDA.**

Q. **How is it that you recognize this?**

A. **I have seen this before. And, also, I have participated in preparing this.**

Q. **Where can I find the formulation for the Exela product**

in this document?

A. **It's on the third page, the Exhibit No. XLA-004579.**

(There followed a portion of the proceedings ordered sealed by the Court. That portion has been transcribed, bound separately, and will be sealed separately.)

MR. BOGGS: Your Honor, I am not sure what the protocol here is for this. But this information that we have just read into the record is still highly confidential, in terms of the formulation, the exact formulation.

I wasn't sure whether there is a mechanism for sealing the record, sealing the transcripts for this part.

THE COURT: We will discuss it, you will remind me.

MR. BOGGS: Okay, I will. Thank you. I just wanted to --

THE COURT: Mr. Maurer, you have the capability.

COURT REPORTER: Yes.

BY MR. BOGGS:

Q. **Dr. Koneru, we just looked at the Exela brimonidine formulation. And you stated previously that your objective was to produce a product that would not infringe the Orange Book patents that cover the Alphagan P .15 percent.**

Do you believe that you satisfied that objective through your reformulated 0.15 percent brimonidine tartrate product?

A. **Yes, I have.**

Q. **And could you explain why?**

A. **Yes. The formulation, we have a pH of 6.7 either during the manufacturing or during the release or what it is**

on stability.

THE COURT: Would you repeat that, Doctor, please? It doesn't exceed 6.7?

THE WITNESS: Either during the manufacturing or during the release. Nor during the shelf life.

BY MR. BOGGS:

Q. Okay. By "shelf life," what pH are you referring to there?

A. The shelf life pH is 5.5 to 6.7.

Q. What is the release pH?

A. The release pH is 6.2 to 6.7.

Q. And what is the manufacturing pH?

A. 6.5 to 6.7.

Q. And here is a slide from my opening. Does that accurately characterize the pH's of the ANDA?

A. Yes.

Q. Now, do these ranges correspond to any geometrical figure?

A. If you use the lower end of the ranges, you could construct a pyramid. 6.5 at the manufacturing is at the top, and then 6.2, the release, and 5.5 in the shelf.

Q. So it is narrow at the top during manufacture and it progressively gets wider. Right?

A. Yes.

Q. So the first pH that you frequently see referred to is

right after it's manufactured. And then you have a broader range at release. Then, of course, the shelf life is even broader. Is that correct?

A. **That's correct.**

Q. **Now, do you have an understanding -- what was your understanding or your belief at the time as to why a product that has a pH that never exceeds 6.7 would not be the same as one with a pH of about 7.0 or greater?**

A. **Well, the product has a solubility profile that is dependent upon pH. In other words, as the pH changes, the solubility changes.**

Also, as the pH changes, the amount of ionized drug versus the unionized drug changes.

A pH of 6.5 will give you a different solubility and ratio of ionized versus unionized compared to the pH of 7.0.

Like that, as you go down each different pH, you will have different amounts. So it will not be the same.

Q. **In designing your product, did you think that your pH in the '834 patent was going to be a problem?**

A. **No. I never felt that way. Like I say, I have read the specification, I have read the claims, and, also, I have read the file history. And I reviewed the prior art. If you look at the .5 percent and the .2 percent product labeling, the prior art products, they have a pH range of**

5.6 to 6.6 ranges. And then in the file history, they mention, they are trying to distinguish their products from the prior art by saying that the Alphagan prior art product, .2 percent, had a pH of 6. -- 6.3 to 6.5, and, also, 6.6 to 6.8.

So I felt that the 6.6 -- 6.7 pH is firmly within the prior art.

Q. **Okay. You mentioned the .5 percent Alphagan NDA, I think.**

A. **Yes.**

Q. **I would like you to turn to EDTX-124. I tried to show you this earlier.**

I would like you to go first to XLA-011932 -- 82, excuse me.

A. **Yes.**

Q. **Do you see that?**

A. **Yes.**

Q. **And what is this document that we are looking at?**

A. **It is part of the NDA approval package. The NDA number is 20-490, which is brimonidine tartrate .5 percent.**

Q. **Okay. What are the ingredients of that formulation?**

A. **The inactive ingredients are polyvinyl alcohol, sodium chloride, sodium citrate dihydrate, citric acid monohydrate, and purified water. They have also used sodium hydroxide and hydrochloric acid for pH adjustment for your targeted**

formulation pH of 6.3 to 6.5.

Q. **Now, do you use any of those ingredients in your formulation?**

A. **Yes. We use the polyvinyl alcohol, sodium chloride, sodium citrate dihydrate, citric acid monohydrate and purified water and sodium oxide and hydrochloric acid.**

THE COURT: Would you say that again, Doctor, a little more slowly.

THE WITNESS: Sorry. Can I just compare my formulation, just to make sure?

THE COURT: Sure.

THE WITNESS: Yes. My formulation, we use polyvinyl alcohol, and we use sodium chloride, sodium citrate, and citric acid.

THE COURT: Is that sodium citrate dihydrate?

THE WITNESS: I believe so, Your Honor. It was abbreviated in here.

THE COURT: Okay. What was the next one?

THE WITNESS: The next one is the citric acid monohydrate. And we used citric acid as abbreviated, also. And purified water. And sodium hydroxide, and/or hydrochloric acid.

THE COURT: Okay.

THE WITNESS: There, it says preservative benzoalkonium chloride --

THE COURT: He can ask another question.

BY MR. BOGGS:

Q. **Dr. Koneru, does your formulation contain a preservative?**

A. **Yes, it does.**

Q. **What is that?**

A. **That's benzyl benzoalkonium chloride.**

Q. **Dr. Koneru, I would like you to turn your document to XLA-012181, if you would.**

THE COURT: What volume are we in now?

MR. BOGGS: It should be the same document, Your Honor.

THE COURT: I am sorry. What is the Bates number?

MR. BOGGS: XLA- --

THE COURT: Just the last three numbers.

MR. BOGGS: 12181.

BY MR. BOGGS:

Q. **Dr. Koneru, what is this?**

A. **This is part of the .5 percent NDA where they are describing the product, the physical properties and its chemical structure and its water solubility.**

Q. **You mentioned water solubility. Where do you see information about that?**

A. **You see the chart down at the bottom of the page.**

Q. **And what does that chart tell you?**

A. **It is giving the solubility of the brimonidine tartrate as a function of pH in water.**

Q. **And the left column is the pH. Is that right?**

A. **Yes.**

Q. **And the right column is the solubility. Is that right?**

A. **Yes.**

Q. **Now, that is in milligrams per milliliter. Is that right?**

A. **That's correct.**

Q. **Can you translate that into percentages?**

A. **Yes. You usually put a zero in the front. So you put the decimal point once.**

Q. **For example, if you looked at 7.00 pH, that would be .01 percent?**

A. **No, .194 percent.**

Q. **I would like you to look at JTX-4, if you would.**

Do you recognize this document?

A. **Yes.**

Q. **I would like you to turn to Table 1 in the patent, Column 4.**

A. **Yes.**

Q. **Tables 1 and 2, do you see those?**

A. **Yes.**

Q. **First of all, what is the '834 patent?**

A. **This is the patent that was asserted against Exela.**

Q. **So this is the patent that you are being sued for patent infringement on. Is that right?**

A. **That's correct.**

Q. **Now, Table 1, what do you see there?**

A. **It's the solubility -- I am sorry. It is the composition of .5 percent brimonidine tartrate in ophthalmic solution.**

Q. **And are all those ingredients the same as those that we just looked at in the NDA, EDTX-124?**

A. **I believe so. Let me double-check.**

I believe it doesn't mention the citric acid.

Q. **Okay. Now, here is Table 2 from the '834 patent. Do you see that?**

A. **Yes.**

Q. **What information is contained in here?**

A. **It is giving the solubility data of brimonidine tartrate in the ophthalmic solution for a pH range of 5 to 8.**

Q. **Now, how do those solubility characteristics compare to those that we saw in the Allergan NDA 2490 in EDTX-124?**

MR. SINGER: Your Honor, is Dr. Koneru being offered as an expert on solubility? It seems we have gone far afield and I am going to interpose an objection.

MR. BOGGS: We are going over the things he considered in formulating --

THE COURT: That is my understanding.

MR. SINGER: With that explanation, thank you.

THE WITNESS: Would you take me back to the Bates number.

BY MR. BOGGS:

Q. **For the NDA?**

A. **Yes.**

Q. **XLA-012181.**

A. **Yes, I see that.**

Q. **Now, do both of these pieces of information tell you that formulating your product at the pH that you did would provide for a solution whereas the brimonidine would have the appropriate solubility characteristics at your desired pH?**

A. **I was interested in the .15 percent brimonidine tartrate solution. And, so, I was looking at the solubility of the brimonidine tartrate .15 percent solution. And it would correspond roughly to, when you look at the milligram per amount, it's 1.5 milliliters per amount.**

From this data, I would say that it's plainly soluble. I don't have any solubility problem.

Q. **Where would the .15 formulation fall in the table on the left?**

A. **It would be between 7.0 and 7.4. 7.00 and 7.40.**

Q. **Be somewhere in there. Is that correct?**

A. **Right.**

Q. **So anything less than that would be what?**

A. **Would be soluble, quite soluble.**

Q. **That's correct.**

Now, this information in XLA-012181, is that publicly available information?

A. **Yes.**

Q. **How is it that we know that?**

A. **I went to the website of the FDA, and you can search on the FDA website for summary business of approvals, the package, the approval package, the approval package summary. From the information that you see here on the top, you see a date, April 17, 1997. And this is a FOIA request, Freedom of Information Services?**

It is a commercial company. They have obtained this document on April 17th, 1997. So it is available at least from that point on publicly.

Q. **Dr. Koneru, you should have a white binder in front of you.**

A. **Yes.**

Q. **Now, this white binder contains some excerpts from the handout that we looked at a larger portion of earlier. Do you have this?**

A. **Yes, I do.**

Q. **The very first page, as you open up the notebook, is that the chart that we were just looking at a little while ago?**

A. **Yes.**

Q. **And that has -- that's designated XLA-004579. And it's the side-by-side comparison with Alphagan P, Exela's product, and the Alphagan .2 percent. Is that correct?**

A. **That's correct.**

Q. **Okay. Now, I would like you to look through this book and tell me if there is anything in here that tells you how to make the .15 percent formulation?**

A. **Yes. I see in Tab 2.**

Q. **Tab 2?**

A. **Yes.**

Q. **If you look at Tab 2, what is the number at the top right of the page? It's not a number, it's a designation. Do you see that?**

A. **Compounding instructions.**

Q. **What is to the right under "lot number"? Do you see that?**

A. **Yes.**

Q. **What is X015, what does that signify to you?**

A. **That is brimonidine tartrate .15 percent in solution.**

Q. **Does that represent anything in particular?**

A. **That represents the Exela exhibit batch number.**

Q. **The batch number. What is a batch?**

A. **A batch is a -- A batch is a product you make for various reasons. You can call them commercial batches, exhibit batches, trial batches, clinical batches. It is a group of products.**

Q. **A group of products for what?**

A. **For whatever purpose. It could be for trial purposes, clinical purposes, it could be for commercial launch, it could be for ANDA purposes, ANDA filing purposes.**

THE COURT: A batch is a commercial run of the product?

THE WITNESS: It's not a commercial size, Your Honor. It can be commercial --

THE COURT: Or a run.

THE WITNESS: A run.

BY MR. BOGGS:

Q. **It is an actual material made. Correct?**

A. **It is actual material, yes.**

Q. **Compounding instructions, what does that mean?**

A. **These are the instructions on actually how to mix the various ingredients of the product.**

Q. **Okay. This tells you how to make it. Is that correct?**

A. **Yes.**

Q. **Okay. Now, if you would, I would simply like you to step through here and tell me how you add all these things together that are mentioned in here and where in this section under Tab 2 things are identified?**

A. **Okay.**

On the front page itself, 6302, you will see the various things about the actual time that has to be done and the temperature for the bulk solution and what precautions the personnel must take. And then the various ingredients that are going to be used and how to handle them.

Then on the next page, you will see the room qualification. It is confirming that the room is ready for manufacturing.

Q. **Dr. Koneru, let me interrupt for a minute. I see writing on this paper. What does that mean to you?**

A. **This is an actual executive batch record. That means people have actually done the work and they have put the code in, the numbers, and they have signed it, verified it with a date and sometimes even the time.**

Q. **Okay. I am sorry. Continue.**

A. **You go on, and you will see various things have been taken care of, like the water projection and the heat exchangers and various things that need to be ready for the batch preparation.**

So you go on, and I used the numbers on the left

side column to practice. You go to, for example, the, probably No. 24. That will be a good starting point for us.

Q. That's 6307.

A. Yes, 6307. You start with the water and add the calcium chloride dihydrate, that would be the first thing to add. It's on the next page.

Item No. 26.

Then it tells you what to do and how long you have to mix it. And you measure the weight of the vessel and all that.

Q. And what is the next thing that you add?

A. Then you add magnesium chloride.

Q. And that's shown where?

A. It's on Item 27.

Q. Okay. What is the next thing that you add?

A. Then you add potassium chloride. That is Item 28.

Q. Item 28?

A. Yes.

Q. That was done. Correct?

A. That was done.

Q. And how do you know that?

A. Because somebody put their initials and then a date on it. It shows it was done on 6/22/06.

Q. What is the next item?

A. The next thing you do is add sodium chloride, which is

Item 29.

Q. **That was done?**

A. **Yes.**

Q. **What is the next thing?**

A. **Then Item 30 is citric acid monohydrate.**

Q. **That was done?**

A. **Yes.**

Q. **And what do you do after that?**

A. **Item 31, you add sodium citrate dihydrate.**

Q. **That was done?**

A. **Yes.**

Q. **The next item?**

A. **Item 32, you add polyvinyl alcohol.**

Then Item 33 --

Q. **I am sorry, Dr. Koneru. What item was the polyvinyl alcohol?**

A. **It's 32.**

Q. **Then what do you do?**

A. **Then you add brimonidine tartrate. That's Item 33.**

Q. **And was that done?**

A. **Yes.**

Q. **Okay. What's in Box 34?**

A. **34 is information on the pH meter. And, because, at 35, Item 35, you will be measuring a pH of the product at the time. And, so, a preparation for that, you have to make**

sure that your pH meter is working properly. It has to be added, what pH meter you use. That is this information here.

Q. **Then you use that pH meter to do what?**

A. **You want to measure the pH of the bulk solution that has been prepared up to that point.**

Q. **Was that done here?**

A. **Yes, it was.**

Q. **And what was it?**

A. **The pH was measured, and it showed a pH of 5.60.**

Q. **Now, at the top of that box, Box 35, it refers to limits. What does that mean?**

A. **That is the specification that we have established, which tells the operator that the pH cannot exceed 6.7.**

Q. **And did you satisfy that limit?**

A. **Yes. As you can see in the table here, there is a checklist here. It says, "pH confirms"? "Yes or no"? And it was checked as "yes."**

Q. **Then, after you checked the pH, what do you do?**

A. **If it confirms -- if it is below 6.7, then you go onto the next step.**

Q. **Okay. What is the next step?**

A. **The next step is add benzoalkonium chloride.**

Q. **By the way, what happens if the pH doesn't meet the specification?**

A. **Then the operator has to notify his or her supervisor.**

Q. **All right. Back to 36. What is that?**

A. **In 36, you add the benzoalkonium chloride.**

Q. **Okay. 37?**

A. **Then you add water.**

Q. **Then 38?**

A. **38, you check the pH of the solution again.**

Q. **Are there any limits associated with that?**

A. **Yes. It says it should be between 6.5 and 6.7.**

Q. **With Batch No. X-015, what was that pH measured at?**

A. **It was measured at 5.6.**

Q. **What is the next step?**

A. **You will see here, the pH is not confirmed to 6.5 to 6.7. It was below that. So the operator has checked no. And then you go to 39.**

39, it says, If the pH is not pyramid, adjust to 6.5 to 6.7 with one normal hydrochloric acid or one normal sodium hydroxide.

And they have page numbers where there are procedures on how to make them.

Q. **So, in this particular batch, the product came out at a pH of, in the middle fives. And you had to raise it up --**

A. **Yes.**

Q. **-- into the range that you wanted. Is that correct?**

A. **That's correct.**

I am aware of here you will see the operator has used sodium hydroxide, 615 mil of it, to raise the pH to 6.6.

Q. **Then what happens?**

A. **Then you go to Item 40, which says, Add some more water. Then go to Item 41 and then 42, you verify the pH again. And you have another spec there, it says, 6.5 to 6.7. And the result shows that it was at 6.7.**

So the operator has checked yes, confirms.

Q. **Okay.**

A. **And then the bulk solution has additional finishing steps that you need to go through. And they are all the way up to Item 50. That concludes the compounding portion.**

Q. **Okay. So that was the compounding portion. Would some people call that the manufacturing portion?**

A. **That's correct.**

Q. **And if you look up on our demonstrative, No. 15, is that the pH that's specified in the ANDA?**

A. **Yes.**

Q. **And, in fact, we just stepped through an actual production of Lot X-015. Isn't that right?**

A. **That's correct.**

Q. **And it met the pH specifications. Correct?**

A. **The manufacturing pH specifications, yes.**

Q. **The manufacturing pH specs, that's right.**

Now, if you would, turn to the next item behind Tab 3. Do you see that?

A. **Yes.**

Q. **What is that?**

A. **This is the finished product test certificate, which is part of the ANDA we filed.**

Q. **Now, does that include a batch number?**

A. **Yes, it includes the batch number.**

Q. **And where is that?**

A. **It's in the middle of the box. It says lot X-01500.**

Q. **Okay. It's also on the next page, too, Batch No. X-01500. Do you see that?**

A. **Yes.**

Q. **What does this particular form tell us?**

A. **This is the list of the specifications and the results of the specifications that the finished product has to have.**

You will see in the middle, it says, Finished product, test summary. And then it comes down to brimonidine tartrate, 1.5 milligrams per amount. And then it has a batch number, and then it has a fill size. We have three different sizes, 5 ml, 10 ml, and 15 ml. This is the information on the five ml bottle size.

Q. **So you took your batch sample, X-01500, and you created smaller samples of 5 mil, 10 mil, and 15 mil bottles?**

A. **Yes. These were already filled in.**

Q. **And you tested them. Is that right?**

A. **Yes. When you are filling the bottle, for final use by the consumer, the product has to meet certain specifications. And there is all the different items that every product has to pass. Otherwise, the product will not be released to the market.**

In the left column, it starts, Appearance, clarity, foreign matter, pH. It goes on, particularity, osmolality, viscosity, et cetera.

Then next to that is, you see the minimum sample is required and method, what method to use, to test that. Then you have the limits of compliance. That tells you what the limits should be.

And then, the next column, you see the results. These are the actual observed results.

Then you have a column that says "pass/fail." And then somebody has to initial it and put a date on it.

Q. **Now, is pH listed on that form?**

A. **Yes, it is.**

Q. **And where do you find that?**

A. **It's the last row on this page.**

Q. **Okay. Last row on this page, okay. What does that line tell us?**

A. **That the pH is one of the specifications, and it has a**

limit of compliance, 6.2 to 6.7. And the result shows 6.7. It looks like there were two samples taken.

One of them had a 6.7. The other one also had a 6.7. Then, right next to it, it says "pass." It is passing because it is falling within this range, in the compliance column.

Q. **This was for Batch No. X-01500. Right?**

A. **That's correct.**

Q. **Now, down at the bottom, it says, "Limit of compliance." Do you see that? What is that range?**

A. **The range is 6.2 to 6.7.**

Q. **What does that correspond to?**

A. **It corresponds to the release pH.**

Q. **That is the second pH that we encounter. Right?**

A. **Yes.**

Q. **So we have the manufacturing pH. We saw that as we were going through the manufacturing protocol. Right?**

A. **Yes.**

Q. **And that was 6.5 to 6.7. Correct?**

A. **That's right.**

Q. **Then we just found the release pH. Right?**

A. **Yes.**

Q. **And that was 6.2 to 6.7?**

A. **That's correct.**

Q. **Now, the next section, under Tab 4, do you see that?**

A. **Yes.**

Q. **What is this?**

A. **This is a document from the ANDA we filed which gives the stability test data.**

Q. **And this was the stability test data for what lot?**

A. **It's lot X-01500.**

Q. **A couple pages in, what is this chart?**

A. **This chart gives you the summary of the stability testing done on Batch No. X-01500.**

Q. **How do we know that?**

A. **Because it says on the left, on the top.**

Q. **The very first line, it says, Batch No. X-015000. Is that right?**

A. **That's correct.**

Q. **What does this table tell us about pH?**

A. **The pH is listed on the sixth row. It has a specification of 5.5 to 6.7. Then it has the various time points where you would measure the pH. And the time is measured in months. And you can see that the pH was measured, and you will see a date there in the bottom, in the box, and you will see that the pH was measured four times here.**

Q. **Now, when you say "four times," that's over a three-month period of time. Is that right?**

A. **Yes. There is a time zero, and then one-month,**

two-month, three-month point.

Q. What information can we derive out of the one-month testing? Describe that one-month testing.

A. Okay. After one month, you take the sample and you measure the pH according to the method listed here, that's following SOP Chem 437. They give you all the details on exactly how to measure, how to calibrate the machine, and all that. Then you see the results. At one month, you have 6.4 pH.

Q. What conditions were those run under?

A. The product was started at 40 degrees C and 75 percent relative humidity. This is called an accelerated stability condition.

Q. So, after one month under 40 degrees in these accelerated conditions, what would that tell you about the shelf life of this product?

A. It's -- you know, usually, shelf life you measure after three months' data.

Q. So you take three months of data and you determine the shelf life?

A. Yes.

Q. Is there a correlation between the accelerated test and the shelf life?

A. Yes. This is usually extrapolated because we wanted to save time on storage. So if the product is stable and

meets all the specifications, after a three-month accelerated stability, then FDA permits you to have a two-year shelf life for the product.

Q. **So, in this particular test, stability testing, these were accelerated tests. Is that right?**

A. **That's correct.**

Q. **And can you tell what the shelf life of the product was after three months?**

A. **It appeared to be that the product was passing all the specifications. So the shelf life should be two years.**

Q. **Two years, okay.**

The lowest the pH got there was 6.2. Is that right?

A. **That's correct.**

Q. **After two years?**

A. **No. That is after three months of accelerated solubility.**

Q. **That's right. But that's equivalent to 6.2 after two years?**

A. **Yes. The product is expected to be like this after two years, at two years.**

Q. **So what are the limits for pH under these conditions?**

A. **The pH specification we have is 5.5 to 6.7.**

Q. **Did Batch No. X-01500 pass the test?**

A. **Yes, it has.**

Q. **All right. Now, we saw that pH range in the stability testing chart. What range does that correspond to?**

A. **That is the shelf life.**

Q. **5.5 to 6.7. Is that correct?**

A. **That's right.**

Q. **Tab 5, what is under Tab 5 in the white book?**

A. **This is part of the ANDA. The document is titled "Stability Summary Report and Specification Rationale Report" for Lot X-01500.**

Q. **That's under Tab 5?**

A. **Yes, sir.**

Q. **And it is still Lot X-01500. Right?**

A. **That's correct.**

Q. **What does this report tell us?**

A. **This says, Summary of the stability data. Then, also, it's the rationale for selecting those specifications. As you go through the document, you will see that it talks about the various parameters, such as appearance, foreign matter, et cetera. First, on the top, you will see the study design. And then it goes through the various parameters.**

The next page, you see color of the solution, pH, particularity matter, on and on. It goes through each and every one of those specifications.

Q. **What does it say about pH?**

A. **The pH's on Exela 007061, it says that the batch samples met the established criteria of 5.5 to 6.7, following the accelerated set of conditions.**

Q. **So it passed the test. Is that right?**

A. **It passed the test.**

Q. **Now, what's under Tab 6?**

A. **Tab 6 is a side-by-side comparison of the package inserts for the reference listed drug and Exela's proposed product.**

Q. **I would like you to look under Tab 1 there.**

A. **Yes.**

Q. **And what is Tab 1?**

A. **It is a stability commitment from the company to the FDA that we will conduct the studies as per the protocol and will test them as per the protocols for 24 months. It talks about how we do the tests. And then it also commits to provide that information as required by the statute, the declarations. Then it says, We commit to withdraw from the market any pharmaceutical outside of the approved specifications for the drug product.**

This is all on paper.

That means if the product fails any of the conditions that are outlined in the specification, the product will be withdrawn from the market.

Q. **In other words, you can't sell the product?**

A. **You cannot sell the product, and, also, any product that is out there sitting on the shelf should be withdrawn, should be recalled.**

THE COURT: Mr. Boggs, where does that letter occur?

MR. BOGGS: This is under Tab 1.

THE COURT: I see. Thank you, sir.

BY MR. BOGGS:

Q. **Dr. Koneru, if you are making the Exela brimonidine product and you don't meet the process specifications, what happens to the product?**

A. **The product should be destroyed.**

MR. BOGGS: May I have a moment, Your Honor?

THE COURT: Yes, sir.

(Pause.)

BY MR. BOGGS:

Q. **Dr. Koneru, you indicated before that you had looked at five patents that were listed in the Orange Book. Do you recall that?**

A. **Yes, I do.**

Q. **And you indicated that one was the '078 patent, and then you referred to four other patents, including the '834 patent, which we recently discussed. Do you recall that?**

A. **Yes, I do.**

Q. **Now, the '078 patent is on the right. Do you see**

that?

A. Yes.

Q. And I take it you looked at that patent. Is that right?

A. Yes, I did.

Q. And you designed the Exela product to avoid infringement of that patent. Is that right?

A. That's correct.

Q. And what is it about, at a minimum, what is it about your formulation that is different than what is required by the '078 patent?

MR. SINGER: Your Honor, for the record, we are not asserting this patent against Dr. Koneru's company. We are just asserting the '834 patent.

THE COURT: Where are we going?

MR. BOGGS: This is just more of the process that he went through in developing his product. He designed the various features.

THE COURT: You don't think you have covered this enough? I am not trying to tell you how to try your case.

MR. BOGGS: Perhaps we can move to something else.

THE COURT: It is up to you. I think Mr. Singer makes the point that this line of inquiry may be largely

irrelevant, if not cumulative, perhaps. But, again, it's your case.

MR. BOGGS: Thank you, Your Honor. I will just move on.

THE COURT: Okay.

Maybe I should say at least cumulative. It's probably relevant. It seems to be, potentially, cumulative.

BY MR. BOGGS:

Q. **Okay. EDTX-103, if you would.**

A. **Which number is this?**

THE COURT: I think that's the next volume, Doc. Is that in 2, Mr. Boggs?

MR. BOGGS: 3. Volume 3.

THE WITNESS: Yes.

THE COURT: Where did he find it? Is it in 2?

THE WITNESS: It is in 2, Your Honor. No, I am sorry. 3.

THE COURT: Here it is.

BY MR. BOGGS:

Q. **Dr. Koneru, efficacy has been raised as an issue with respect to your product. Do you agree?**

A. **Yes.**

Q. **Now, originally, you mentioned that you reviewed a paper called the Walters paper. Do you remember saying that?**

A. **Yes.**

Q. **Is this the Walters paper?**

A. **Yes, it is.**

Q. **How is it that this paper is relevant to your design of your product?**

A. **This paper is from 1996. It was published in 1996.**

This talks about various concentrations of brimonidine and their effectiveness and safety and dose response and dosing studies. That's what the title says.

Then you go in there, and you will see Figure 3.

The study was conducted for 28 days. And the concentrations of brimonidine are listed here. The very bottom curve is the.5 percent. That is the highest strength.

Then the one up is the.2 percent. Then one up is 0.08 percent. And all the way at the top is the placebo, the vehicle.

Q. **When you are saying the "top," you are talking about the top line that runs from the left to the right?**

A. **That's correct.**

Q. **Then the next line down is the .08 percent. Then the next line is the .2 percent. Then the next line is the .5 percent?**

A. **That's correct.**

Q. **What is being measured here?**

A. **The measurement is the introduction to the intraocular pressure.**

Q. **What does the 0 represent, the .0?**

A. **On the x axis, which is on the horizontal axis, there is a time. On the y axis, you will see the measurement of IOP in milliliters of Mercury. The zero is the day zero, the first day.**

That's where it was before the drug was administered.

Q. **And 7 and 14, 21, and 28, those are all days?**

A. **Those are all days.**

Q. **What are the numbers on the left side?**

A. **The left side is the measurement of the IOP for patients. And you see the number 25, 27, and 23, and 21. They are all considered to be relatively high numbers. That means if a person has, let's say, an IOP measurement of 25, the person maybe tends to be having glaucoma.**

Q. **And then you want a -- a good number is a much lower number. Is that right?**

A. **Yes. A good number is definitely lower. 17 is definitely a good number. But depending on who you talk to, sometimes 21 is a good number. And sometimes even 23 is a good number. There are cases where I have read that the IOP can go up to 30, 35, also.**

Q. **So the objective here is to lower intraocular**

pressure. Is that right?
A. That's correct.
Q. So there is a drop. And that drop, the bigger the drop, the better. Is that right?
A. Yes.
Q. So the .2 percent formulation, do you know what that was?
A. Well, the .2 percent, it looks like it came down to 20, on the first time point. Then it went up a little bit, but then kind of stabilized, and it merged with the .5 percent from Day 14 on. So that tells me that after 14 days, the treatment with .5 percent and the treatment of the .2 percent were right angle.
Q. The .2 percent formulation, was that Alphagan?
A. That's correct.
Q. That was the original Alphagan product?
A. I believe so, based on the date of the publication.
Q. And the excipients, what were the excipients of the original Alphagan product, the vehicle?
A. The excipients were the polyvinyl alcohol and the citrate buffer and benzoalkonium chloride as a preservative.
Q. Okay. So it had the same preservative as you were planning to use, the same thickener that you were planning to use, the same buffer; is that right?
A. That's correct.

Q. **All right. The concentration that you were planning on using, what was that?**

A. **.15 percent.**

Q. **.15. Where would that fall in this graph, if you were to estimate its presence?**

A. **That would be roughly between the .08 and the .2 percent.**

Q. **Now, all of these formulations, the .08, .2, .5, they all had the polyvinyl alcohol as the viscosity enhancer, they had the benzoalkonium chloride as the preservative, and they all had the citrate buffer. Is that right?**

A. **That's probably right. I couldn't confirm, because they haven't given the formulation here in the paper. But based on the NDA for the 12.5 percent and also the NDA for the .2 percent, that was the only type of formulation that was available at the time.**

Q. **Now, the .5 percent, you mentioned the NDA for that. That's the one that we looked at before. Is that right?**

A. **That's correct.**

Q. **And we were looking at the solubility data. Is that right?**

A. **That's correct.**

Q. **And it was that solubility data that would indicate that a .15 percent formulation would be soluble without a solubility enhancer at pH below 7. Right?**

A. **That's correct. In fact, if I can take you to the patent, the '834 patent, I can -- that also gives the indication that you don't need a solubility enhancing component for the .15 percent.**

Q. **Where on the '834 patent?**

A. **You can focus on this graph here. You will see on the white axis, the solubility is given.**

There is a concentration of the brimonidine here. The scale is in ppm. That roughly corresponds to about, you know, the best way to get to the data is you put a zero in the front -- you put a decimal point in the front. So, here, 1500 ppm, that roughly corresponds, is the .15 percent.

If you want to see the solubility of this, you follow this curve, and you look at the pH. They have 7.0 pH, the 1500 ppm, which is .15 percent, is clearly soluble. There is no solubility issue here.

And the product that we were going to make would have a pH of 6.7 or less, so I have no worries about solubility.

Q. **At what point do you need the solubility enhancer?**

A. **For a .15 percent, if you were going about here, let's say, 7.5 pH, or 7.4, from that point on, I think you need a solubility enhancing component, according to this graph.**

Q. **Can you point in the patent where it discusses the**

solubility enhancers?

A. **Yes. It mentions about the solubility enhancing component at several different places. You can start with the abstract, on the face of the patent.**

MR. SINGER: Your Honor, for the record, we are not asserting those patents against Dr. Koneru and Exela, either, just for the record. I didn't know if that was relevant examination. I thought we were talking about what he considered with respect to a solution. But we are not asserting the solubility component patents against Exela.

MR. BOGGS: It is more background. How he designed his formulation, how he was able to do without the solubility enhancer. You know, of course, you have to know --

THE COURT: I think that going to be helpful to me. We did hear from Allergan at some length about its development.

MR. SINGER: If the Court finds it helpful, absolutely, Your Honor.

THE WITNESS: As I read through the specification, solubility enhancing component was mentioned several different places. It looks like almost about 30, 40 percent of the specification was about solubility enhancing components. And they describe various of them, polyanionic components, and various other polymers, on and on. Then

they also talked about cyclodextrins.

Q. Can you point to where you are looking, Doctor?

A. Yes. There are numerous places. I just want to save some time. In Column 5 -- I am sorry, Column 6, you will see them, starting from Line 17. It goes on through Column 8, and all the way to Column 9, through Line 22.

Then again, it goes to Column 11, talks about SECs again. And, also, you will see the summary of the invention, Column 2, Line 9. It was the first paragraph, the paragraph there, then it goes into the -- it starts at Column 2, Line 52, 53, all the way to the next column.

So this is really, when you read this, you come away with the impression that you need to have a solubility enhancing component to make the brimonidine soluble at pH's of about 7.0 or greater. And they haven't really -- I am trying to find a way to see if there is anything described that you don't need to use a solubility enhancing component to make it soluble. And I didn't find it.

So my impression was that to make a brimonidine tartrate soluble at a pH of 7.0 or greater, you have to have a solubility enhancing component.

But then when I looked at the chart, if my pH was below 7, it tells me, their own data tells me that I don't need an SEC.

Q. Solubility enhancing component. Is that right, an

SEC?
A. That's correct.
Q. Okay. Dr. Koneru, you designed your product, you worked Dr. Nitra in India. You did a lot of development work. You teamed up with Paddock. And then, ultimately, you filed your ANDA. Is that right?
A. That's correct.
Q. Okay. Now, I have put up EDTX-164. Do you see that?
A. Yes, I see that.
Q. What is this?
A. That's a notification letter from Exela to Allergan about the filing of the ANDA.
Q. How is it that you recognize it?
A. This is the document I signed, and sent to Allergan.
Q. That you signed?
A. I believe I did. Let me double-check.
THE COURT: That's what he said. He signed it.
MR. BOGGS: I thought he said he had to double-check.
THE COURT: He said he signed it.
MR. BOGGS: Okay.
BY MR. BOGGS:
Q. What is the purpose of this letter, Dr. Koneru?
A. This is a notification that an ANDA has been filed and we seek approval for the ANDA before the list of patents are

going to expire. This is a statutory requirement that we send a notification to the brand company, and it also explains why we don't think, why we don't believe, we do not infringe the patents or the patents are invalid or not enforceable. And, also, it makes an offer to Allergan, offer of confidentiality so that they can inspect our ANDA. I believe it also offers our product for inspection so they can take our product and test it and then check and see for themselves that we don't infringe.

Q. Was that ever done?

A. I do not believe that the confidentiality was signed, at least before the lawsuit was filed.

Q. So, in Paragraph 2 of the letter, you say the ANDA number is 78-590. That is the ANDA at issue here. Is that right?

A. That's correct.

Q. And in Paragraph 3, there you identify the RLD. Correct?

A. That's correct.

Q. The reference listed drug?

Paragraph 4, you identify the active ingredients. And then Paragraph 5, you identify the patents that are listed in the Orange Book. Right?

A. That's correct.

Q. There you see the '078, '873, '210, '834, and '337

patents listed. Do you see that?
A. That's correct.
Q. And you are currently being sued on the '834 patent of those five. Is that right?
A. That's correct.
Q. Was there anything attached to this letter?
A. Yes. There were two attachments. One was a detailed statement of the factual and legal basis. The other one is the offer of confidential access.
Q. So, what was in the detailed statement, generally?
A. This is a statement of facts, and the, our reasoning as to why we don't infringe these patents. It's extremely detailed as to why we believe we don't infringe those patents, or the patents are invalid.
Q. And that is in -- we just put Page 1 up on the screen. Is that right?
A. Yes.
Q. How many pages was that document, Doctor?
A. This is 47 pages.
Q. 47 pages. You explained your position of noninfringement and invalidity in 47 pages. Is that right?
A. That's correct.
Q. And, then, can you find the offer of confidential access?
A. Yes, I did.

Q. **So, this, you also attached. Is that right?**

A. **That's correct.**

Q. **Did anybody from Allergan contact you before you were sued?**

A. **I do not believe so.**

Q. **Next page. Now, I see a signature on there. Whose signature is that?**

A. **That's my signature.**

Q. **So, you signed the offer of confidentiality in advance, or at the same time that you mailed out ^ your own letter. Is that right?**

A. **That's correct.**

Q. **So you were ready to show them what you were doing and get their blessing. Is that right?**

A. **That's correct.**

Q. **Now, where were you sued initially?**

A. **I believe we were sued in California, District Court in California.**

Q. **In California?**

A. **I believe so, yes.**

Q. **Dr. Koneru, how many times have you had your deposition taken in this case?**

A. **Three times.**

Q. **Three times?**

A. **That's right.**

Q. **How long after the suit was filed before your first deposition?**

A. **I believe it was a month or so after the lawsuit was filed.**

Q. **Right after the lawsuit was filed. What was the purpose of that deposition?**

A. **As I understood it, it was to find out what my company is, what I do, and how the company is formed, that sort of thing.**

MR. BOGGS: Just a moment, Your Honor.

(Pause.)

MR. BOGGS: Your Honor, we don't have any further questions.

THE COURT: All right. Counsel, how are we doing on time?

MR. SINGER: I have got about, I was wondering if I could have a bio break, actually. I have about 40 minutes of cross-examination.

THE COURT: I mean overall in the case. I have a sense we are a little ahead of schedule. Is that fair?

MR. BOGGS: Yes.

MR. BREISBLATT: Your Honor, I am making a quick estimate. I don't know how long crosses are going to take. Based on my talking, it sounds like Exela will probably finish its case sometime tomorrow. We will put on

Dr. Banker, may run over to Monday. Then I believe, how many more witnesses do you have after that?

MS. BROOKS: Two to three, Your Honor. Which I think we could wrap up in a day.

MR. BREISBLATT: I think what we are talking about, the Court gave us until Wednesday. I think we are going to meet that schedule.

THE COURT: All right. Let's break a little early today. Let's recess.

(Court recessed at 4:42 p.m.)